PREVALENCE AND CLINICAL STUDY OF HEPATITIS B IN ANTENATAL WOMEN

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CERTIFICATE

This is to certify that the dissertation entitled '**Prevalence and clinical study of Hepatitis B in antenatal women'** is a bonafide work done by **Dr.A.Anusha raaj** in the Institute of Obstetrics and Gynaecology (Madras Medical College) Egmore, Chennai in partial fulfillment of the university rules and regulations for award of MD degree in Obstetrics and Gynaecology under my guidance and supervision during the academic year 2009-2012.

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DECLARATION

I solemnly declare that this dissertation entitled **"PREVALENCE AND CLINICAL STUDY OF HEPATITIS B IN ANTENATAL WOMEN"** was done by me at Institute of Obsterics & Gynaecology, Madras Medical College during 2009-2012 under the guidance and supervision of, **Prof.Dr.M.MOHANAMBAL MD.,DGO** and **Prof.Dr.K.NARAYANASAMY, MD.,DM.** This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Degree in Obstetrics and Gynaecology (Branch-II).

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INTRODUCTION

Hepatitis B virus occurs worldwide and constitutes a serious public problem. According to WHO, HBV infection is 100 times more lethal than HIV and therefore requires more attention. Despite availability of a vaccine, HBV infection is endemic, estimated to affect 400million people worldwide with very high carriage rate (up to 20%) particularly in south and East Asia. Worldwide vertical transmission remains the most frequent route of infection particularly in endemic areas where up to 20% of women of childbearing age may have HBV.

These women constitute a reservoir of perinatal transmission, which is associated with a very high rate of chronicity (up to 90%)in infants when HBsAg and HBeAg is positive. Transmission of HBV can be prevented by vaccination of infants. But despite prophylaxis perinatal transmission of HBV occurs in a small proportion of infants who receive complete active-passive immunisation. High maternal viraemia and HbeAg positivity has been associated with intrapartum transmission and vaccine breakthrough. Antiviral therapy during the third trimester of pregnancy in high riskwomen with chronic HBV infection reduces viral load in the mother and decrease the risk of transmission, although data are lacking. Safety data in pregnancy are most robust with LAMIVUDINE and TENOFOVIR compared with other therapies. Hence effective maternal screening and immunoprophylaxis of neonates remains the best method of prevention of mother to child transmission.

PREVALENCE AND CLINICAL STUDY OF HEPATITIS B IN ANTENATAL WOMEN ATTENDING OUT PATIENT CLINIC AT INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

AIMS AND OBJECTIVES

1. To study the prevalence of Hepatitis B in antenatal population

2. To study the course of disease,maternal and perinatal outcome in Hepatitis B positive patients.

STUDY CENTRE

Institute of Obstetrics and Gynaecology, Egmore, Chennai – 600 008.

Collaborating Units Dept of HEPATOLOGY, MMC

DESIGN

Cross sectional study

PERIOD

March 2010- Feb 2011

REVIEW OF LITERATURE

HEPATITIS B VIRUS

It is the causative agent of what used to be previously called as Serum Hepatitis or 90 day Hepatitis. It is the smallest double stranded DNA virus known to infect man and is the prototype of the Hepadna virus family which includes similar viruses infecting ducks(DHBV),ground squirrels(GSHV) and woodchucks(WHV).it has the propensity to infect and replicate in the hepatocytes but appears to have intrinsic cytopathic activity. HBV gains far more importance than other forms of hepatitis for its propencity for chronicity and malignant potential(1,2). It is a type 1 carcinogen.

HISTORICAL BACKGROUND:

HEPATO-TROPIC means primarily affecting the liver.

HIPPOCRATES in the 8^{th} century suggested the infectious nature of HBV.

By 1885, hepatitis was found to be transmittable through blood transfusion and syringes when epidemics of jaundice broke out in war victims.

During world war II, between 1939-1945 a series of outbreaks occurred after vaccination for measles and yellow fever implying further that the virus was blood-borne.

In 1947, MACCALLUM classified viral hepatitis into two types: viral hepatitis A or infectious hepatitis, viral hepatitis B or serum hepatitis.

In 1965, BLUMBERG discovers Australia antigen (HBsAg) in Aborigines and showed presence of antigen at high frequency in patients with leukemia and children of Down syndrome.

In 1968, PRINCE & OKOCHI isolated the Australia antigen in Hepatitis B patients and from this information along with discovery of DANE particle in 1970, the first vaccine for Hepatitis B was produced in 1981 and licensed as HEPTAVAX

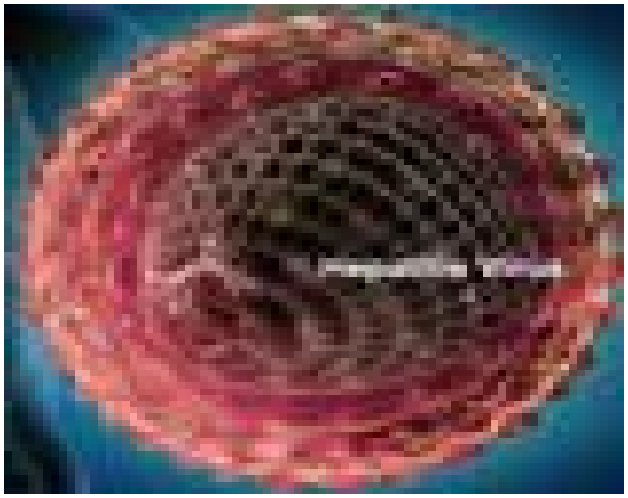
In 1972, HBeAg was discovered

More than a decade later, the nation wide vaccination program on newborns in Taiwan originally launched in 1984 showed successful results, with decrease in annual incidence of hepatocellular carcinoma in children.

STRUCTURE OF HBV

HBV is a complex, 42nm double shelled DNA virus, originally known as the **"DANE particle".**

It has a lipoprotein coat and a nucleocapsid core. The lipoprotein coat is composed of the hepatitis B surface antigen (HBsAg). The nucleocapsid is 27nm in diameter and has a distinct antigen specificity (HBcAg) along with a partially double stranded DNA molecule and an endogenous DNA polymerase enzyme.

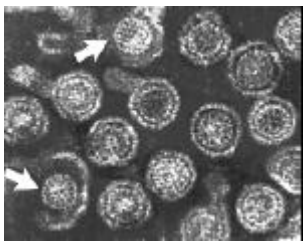


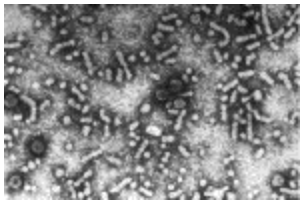
Electron microscopy of Hepatitis B positive serum reveals 3 morphologically distinct forms:

1. Small spherical particles with an average diameter of 22nm, these are antigenic and stimulate the production of surface antibodies. They outnumber the 42nm virions in the serum. The purified 22nm particles are used in the preparation of hepatitis B vaccine.

2. Complete 42nm virion (DANE particle), which represents the intact HBV virion. Of the three morphological forms it is considered to be infectious. The envelope protein expressed on the outer surface of the virion and the 22nm spherical particles is referred to as hepatitis B surface antigen (HBsAg).

3. The intact 42nm virion contains a 27nm nucleocapsid core particle. The nucleocapsid core contains two immunologically distinct antigens, hepatitis B core antigen (HBcAg) and hepatitis B e antigen (HBeAg).





HBV GENOME

Inside the core of the virion is present the viral genome consisting of HBV DNA and DNA polymerase.The endogenous DNA polymerase have partially double stranded and partially single stranded genomes. They rely on a replicative strategy unique among DNA virus but typical of retroviruses. Instead of DNA replication directly from a DNA template, they rely on reverse transcription effected by the DNA polymerase of minus strand DNA from a "pregenomic" RNA intermediate. Then a plus strand DNA is transcribed from the minus strand DNA template by the DNA dependant DNA polymerase and converted in the hepatocyte nucleus into a covalently closed circular DNA, with serves as a template for messenger RNA and Pregenomic RNA. Viral proteins are translated by the messenger RNA, and the proteins and genome are packaged into virions and secreted from the Hepotocyte.

HBV DNA codes for four sets of viral products with a complex, multiparticle structure. Its compact genomic structure, with overlapping genes, permits HBV to code for multiple proteins.

HBV achieves its genomic economy by relying on an effiicient strategy of encoding proteins from four overlapping genes: S,C,P & X and four partly overlapping open reading frames.

PreS1/PreS2/S gene encoding the Hepatitis B surface protein (HBsAg); the pre core/ core gene encoding the Hepatitis B e antigen(HBeAg) and Hepatitis B c protein(HBcAg).the P geneencoding the polymerase proteins and the X gene encoding the X proteins- HBxAg(3).

The HBe protein is able to cross the placenta, it may make the T cells of the fetus tolerant of the HBc protein, thus preventing a cytotoxic T cell response. The HBxAg is capable of transactivating the transcription of both viral and cellular genes. In the cytoplasm, HBxAg effects calcium release, which activates signal-transduction pathways that lead to stimulation of HBV reverse transcription and HBV DNA replication. Such transactivation may enhance the replication of HBV leading to the clinical association between the virus and the protein.

HBV GENOTYPES AND MUTANTS

The HBV genome is heterogeneous and can be classified into 8 genotypes : A,B,C,D,E,F,G and H. currently HBV genotype are defined based on at least 8% divergence across the complete genomic sequence and less than 4% intra-genotypic divergence(4).HBV genotypes are known to be geographically segregated (5). Genotype A is found primarily in North America, Northern Europe, India, and Africa. Genotype B and C are common in Asia; genotype D, in southern Europe, the Middle East, and India; genotype E, in West Africa and South Africa; genotype F, in South and Central America; genotype G, in the United States and Europe (6). Genotype H was recently identified in individuals from Central America and California (7). Several

genotypes may be associated with the severity of the disease but the relationshipbetween the genotype and the developing hepatocellular carcinoma has not been established. In China and Japan, some studies have found more severe liver disease to be associated with genotype C than compare with genotype B (8), other studies have found no such association (9,10). There is some evidence that shows HBeAg seroconversion occurs at a younger age among individuals infected with genotype B (8,10,11). Genotype D has been associated with anti-HBe-positive chronic hepatitis B infection in theMediterranean region (12).

HBV has a reported mutation rate of 10 times greater compare with other DNA viruses. These mutations can occur naturally as well as due to selective pressure from antiviral therapy. There are five clinically relevant HBV types: wild-type HBV, precore mutants, core promoter mutants, tyrosine-methionine-aspartateaspartate (YMDD) mutants induced by lamivudine treatment, and asparagine to threonine (rtN236T) mutants recently identified in patients with adefovir treatment.

In a study carried out in the United States, the precore variant of HBV was rarely found in association with genotype A, but it was found in almost 50% of those with genotype C and in >70% of individuals with genotype D. Those with precore variant and core promoter mutations had higher HBV DNA levels in sera than those persons without these mutations. It is observed that flares in chronic HBV have been associated with increases in concentrations of precore mutation in proportion to wildtype HBV. Exacerbations have been thought to subside with time when the genetic heterogeneity disappears and

patients become exclusively infected with precore HBV. During the treatment of chronic hepatitis B by lamivudine, drug resistance may develop, which is mediated by point mutations with the YMDD motif at the catalytic center of the viral reverse transcriptase. With increase in the mutant viral load, patients can sustain further liver injury. The YMDD mutant level will decrease after stopping lamivudine. Viral mutation also occurs in patients on adefovir treatment during their second year therapy at the rate of 2.5%. The mutation has been reported as asparagine to threonine mutation (rtN236T), downstream of the YMDD motif. It is not clear yet if rtN236T mutant can induce further liver damage.

The hepatitis B virus has 3 distinct antigens:

SURFACE ANTIGEN (HBsAg),CORE ANTIGEN (HBcAg) and E ANTIGEN (HBeAg)

They stimulate corresponding antibody production in most affected individuals.

HBsAg exhibits antigenic diversity. It has

- A group specific antigen – a
- Type specific antigens (d-y), (w-r)

Thus there are four major subtypes of HBsAg adw,adr,ayw and ayr. HBsAg is demonstrable upto 6 weeks and usually disappear 6 – 12 weeks thereafter. Presence of HBeAg in serum is associated with infectivity in HBV and its replication. HBeAg correlates with HBV specific DNA polymerase activity

and is an indicator of viral load. There is a 85% chance of infants becoming susceptible to HBV if mother is HBeAg+ve. If HBeAg persists for more than 8 weeks recovery is delayed and can go in for chronicity.

HBs ANTIGEN IN LIVER

The virion envelope and the HBs particles are synthesized and assembled at the membrane of the Endoplasmic reticulum. From the ER the particles are transported and excreted by vesicles. However when the largest of the 3 HBs proteins (LHBs) is overproduced in comparison with the smaller HBs protein, filamentous particles are formed that are retained in the Endoplasmic reticulum. This may lead to accumulation of HBs protein to the point that the Endoplasmic reticulum becomes dilated. In light microscopy, such large HBs storing hepatocytes appear opaque like ground glass.

CORE ANTIGEN IN LIVER

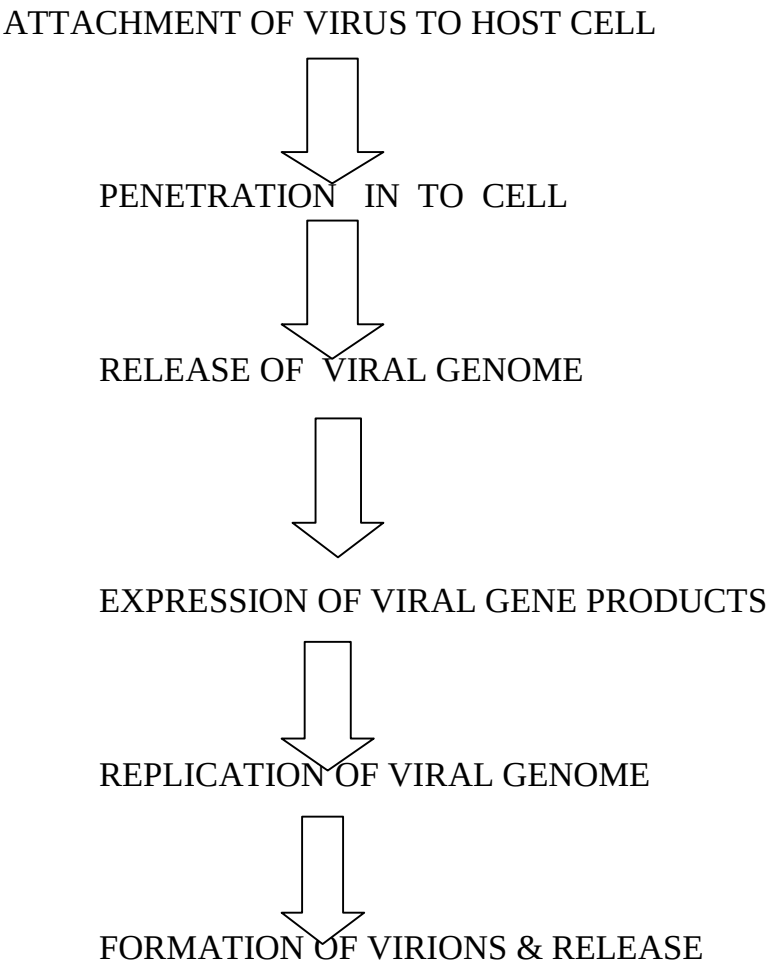
The core particles are synthesized and assembled independently from the HBs proteins. Thereafter they probably attach to patches of HBs protein in ER membrane. By enclosing the whole core particle the HBs protein would mediate budding of the virions to the ER lumen. Non enveloped core particles of human HBV are found in the nucleus where they are stored. In highly viremic individuals without high disease activity all hepatocyte may contain considerable core particles. Non enveloped core particles are not detectable in the serum. Certain HBV product cell lines secretes not only virions, HBs but also core particles.

HBV CARRIER STATE

Persons possessing Hepatitis B surface Antigen in blood for more than 6 months are called chronic or persistent carriers. Carrier state is lifelong and may be associated with mild liver damage varying from minor changes in liver function to chronic active hepatitis, cirrhosis and carcinoma (11). Those with low levels of HBsAg and absence of HBV and DNA polymerase possess very low infectivity are termed as simple carriers (11).

LIFE CYCLE OF HEPATITIS B VIRUS:

The hepatitis B virus encompasses six stages beginning from entry into the host to release of progeny virions



GLOBAL SCENARIO (13)

Hepatitis B is endemic throughout the world, especially in tropical and developing countries. Its prevalence varies from country to country and depends on a complex mix of behavioural, environmental and host factors. In general it is lowest in countries or areas of high standards of living.

The HBV infection is a global problem, with 66% of all the world's population living in areas where there are high levels of infection. More than 2 billion people worldwide have evidence of past or current HBV infection and 350 million are chronic carriers of the virus, which is harboured in the liver, and causes an estimated 600,000 deaths from cirrhosis of liver and hepatocellular carcinoma. The virus causes 60-80% of all primary liver cancer. Between 5% and 10% of adults and upto 90% of infants infected with HBV become carriers. Among these, 25% in the long term develop liver disease.

Hepatitis B is endemic in China and other parts of Asia . In these regions 8-10% of the adult population are chronically infected. In the middle east and Indian subcontinent, an estimated 2-5% of general population is chronically infected. In western Europe and north America less than 1% population is infected.

Based on the different HBsAg carrier states, countries can be divided into three categories: high endemicity (> 8%), intermediate endemicity (>2 – 8 %) and low endemicity (< 2%). Countries or regions can be divided into three epidemiological patterns.

GEOGRAPHICAL DISTRIBUTION OF HBsAg prevalence

LOW (<2%)	INTERMEDIATE (2-8%)	HIGH (>8%)
AUSTRALIA	INDIA	OTHER PARTS OF AFRICA
NEW ZEALAND	NORTH AFRICA	CHINA & MIDDLE EAST
NORTH AMERICA	OTHER PARTS OF EUROPE	PACIFIC ISLANDS
WESTERN EUROPE	JAPAN AND USSR	SOUTH AMERICA

INDIAN SCENARIO (13)

India falls in the intermediate zone of prevalence ranging between 2 to 8%. There are an estimated 43 million estimated HBV carriers in India. 10% of them are HBeAg positive. The HBV carrier pool has increased from 38 million to 43 million over a period of one decade.

An analysis of 191 reports from india using ELISA revealed HBsAg carrier rate to range from 1.10% to 13.1%. the mean of these reports places the national HBsAg carrier rate at 4.7% out of which HBeAg positivity was 24.43% and anti HBeAg positivity was 39.2%. (10,11)

The HBsAg subtype reports have revealed an interesting pattern. In North India including Bombay ‘ayw’ subtype seems to predominate (59.1%). However in South India ‘ad’ aubtype predominates (56.5 – 68.7%). Even with the ad subtype adw seems to be prevalent in the whole of North India and Kerala on the other hand ‘adr’ was the major subtype in Tamil Nadu.

PREVALENCE RATE OF IN GENERAL POPULATION IN DIFFERENT STATES

UTTAR PRADESH	6.05%	HIMACHAL PRADESH	3.26%
KARNATAKA	5%	KERALA	1.39%
TAMIL NADU	4.69%	DELHI	1.39%
MAHARASHTRA	3%	CHANDIGARH	2.4%
RAJASTHAN	1.6%	WEST BENGAL	2.29%

HEPATITIS B AND PREGNANCY (13)

The rate of positivity for HBsAg in pregnant women reported in the Indian literature varies from 0.2% to 7.1% with a weighted average of 2.8%. In larger studies among carrier females about 5 – 12% have been positive for both HBsAg and HBeAg.

The state wise prevalence rates of HBV carriers among pregnant women, Kerala 7.3%, Karnataka 5%, U.P 4.8%, Tamil Nadu 3.9%. a study in North India showed 3.7% HBV carrier rate among pregnant women and 7.8% HBeAg positivity in HBsAg carriers. The report in vertical transmission of hepatitis B in Northern India shows 2.48% positive mothers for HBsAg and 10.3% positivity for babies at birth. In HBeAg positive mothers the babies were at greatest risk with 70 to 100% infection rate and 17.30% if the mother was HBsAg alone. If the mother was anti HBe positive the baby had only 12.20% chance of getting infected.

EPIDEMIOLOGICAL DETERMINANTS (13)

Agent factors

Of the three morphological forms, only the DANE particle is considered infectious.

Reservoir of infection

Hepatitis B carrier state act as natural reservoir as there are no animal carriers for the virus. Risk of chronicity is inversely proportional to the age at which infection occurs. More than 90% chronicity occurs in infancy in contrast to 5-10% in adults as it is apparent that infection in infancy and early childhood is essential for maintenance of HBV infection pool in a population.

Source

A chronic carrier act as a highly infectious source. The level of infectivity varies, from less than 10 virions per ml to 10 to the power of 8 virions per ml, cases may range from inapparent to symptomatic cases.

In HBV carrier pregnant females, antibody to the ‘e’ antigen does not indicate a noninfectious state as a significant proportion of such mothers have high levels of viral HBV DNA sequences in their serum and are potentially infectious.

Infective material

Contaminated blood is the main source of infection, although the virus has been found in body secretions. 0.0001 ml of contaminated blood when comes in contact with intact skin act as a potential source of infection.

MODE OF TRANSMISSION

- Sexual transmission occurs in unvaccinated homosexual men and correlates with multiple partners and unprotected anal sex. Transmission also occurs after heterosexual contact (e.g. 18% infection rates for regular partners of patients with acute hepatitis B) . sex workers are at high risk.(14-23)

- Other routes are: parenteral (blood, blood products, drug users sharing needles and syringes, needle-stick), vertical (infected mother to infant) and oro-anal sex.(14-26)

- Sporadic infection occurs in people without apparent risk factors, in institutions for the mentally disabled and also in children in countries of high endemicity (27,28). Overall, HBV is much more transmissible than HIV.

RISK FACTORS FOR HBV TRANSMISSION:

- Ethnic and genetic predisposition
- Low socioeconomic status, poor hygiene, sanitation and overcrowding
- Exposure to blood products

- Percutaneous exposure to infected blood (health care personnel, drug abusers, tattooing.)

- Homosexual and heterosexual contact
- Immunocompromised and hemodialysis patients

With reference to age it was reviewed by many authors namely J. Shanmugam et al., 1981, D Pal et al., 1991 and Kenneth et al., 1995 incidence is highest among young people between 16-30yrs.

Regarding sex, HBV infection in twice more common in males than females revealed by D Pal et al., 1991., G.Pellizzer et al., 1994 and probably because of a more promiscuous nature of the males.

VERTICAL TRANSMISSION OF HBV

Maternal transmission of an infectious agent can be defined as the direct transfer of the agent from the mother to the child either during pregnancy transplacentally or at the time of birth during delivery. Mothers with acute infection in the 1^{st} and 2^{nd} trimester transmit the infection to approximately 10% of their new born, when acute infection occurs in the 3^{rd} trimester 80 to 90% of the new born are infected.

Mechanism of maternal transmission:

1. In utero infection
2. Perinatal transmission

In utero infection

Intra uterine transmission of viral hepatitis had been suggested by stokes et al., who first reported neonatal infection. Studies have shown that the infant does not become infected if hepatitis occurs early in pregnancy. As pregnancy progresses, the placenta becomes porous, allowing both fetomaternal and maternal hemorrhages. It appears that this leakage is the major cause of intra uterine infection with HBV during maternal viraemia whether the infant is infected in utero or postnatally. If the mother is positive for HBeAg positive the baby has a 85-90% chance of developing chronic HBV infection.

According to Goldeau et al, transmission of Hepatitis B virus to the fetus or newborn is more likely to occur when maternal infection occurs during 2 to 3 months preceding delivery. In such cases antigenemia may develop in 40-50% of babies of which only a small percentage of whom will eventually clear the virus. Placental transfer of Hepatitis B is thought to be rare.

Intra uterine transmission occurs only in 5 to 8% of the infants born to HBsAg the carriers where as most infection occur perinatally (Otto et al.,).

Perinatal transmission:

Transmission can take place during,

- Materno fetal transfusion
- Ingestion of maternal blood, blood contaminated liquor, or other HBeAg containing body fluids during delivery

Lee et al, demonstrated the presence of HBsAg in 17 out 0f 52 (32.7%) samples of amniotic fluid extracted at 37 weeks, in 57 out of 58 (95.4%) samples of gastric fluid aspirated from babies during resuscitation. Thereby proving the direct evidence for the oral route of infection from carrier mothers during delivery. Though 95.3% of the babies had the evidence of ingesting viral antigen, only 70.3% subsequently became HBsAg positive.

Presence of HBsAg in cord blood does not necessarily indicate another infection as it may represent transient maternally derived antigenemia. Perinatal infection is much more frequent when the mother carries both the surface antigen (HBsAg) and ‘e’ antigen (HBeAg) of the virus. In many instances babies with positive cord blood specimen become negative shortly after birth. Persistent antigenemia is affected by maternal antibody titre and antigenemia in siblings. Antigenemia that developed in the first six months of life suggests transmission at birth. Infants who develop chronic HBsAg carriage due to perinatal infection are sources of continuous exposure to siblings and the rest of population.

The relative contribution of hematogenous infection to neonatal acquisition and the contact with maternal blood and vaginal secretions during delivery has not been completely elucidated. For that reason the use of caesarean delivery for the prevention of neonatal infection is controversial. Transplacental leakage of blood or micro transfusion during labour rather than exposure in the birth canal appears to be a major mode of transmission. Thus risk of transmission is significantly lower when elective caesarean section is

done before onset of labour whereas LSCS after onset of labour does not lower transmission.

Infants born to HBsAg positive mothers need not be isolated at birth. However the mothers secretions should be considered potentially infectious and managed with universal precautions. Risk of transmission is greatest if the mother has a history of transmission to her previous children. There are no teratogenic syndromes associated with HBsAg in pregnancy and outcome of pregnancies complicated by HBsAg are no different than those of other women in the same population. Boxall in 1974 detected the presence of HBsAg in breast milk. It is possible that infection may be transmitted postnatally either by virus present in milk or infectious serum from the cracked nipple.

INCUBATION PERIOD

30 to 180 days. Lower doses of the virus result often in longer incubation period. The average incubation period is about 75 days (13).

STAGES OF HBV INFECTION

An individual can develop hepatitis B infection that is acute and achieve complete immune clearance of virus yielding lifelong immunity; however, an alternate fate of the host is the development of chronic hepatitis B. there are 3 stages of HBV infection based on viral host interaction,

1. Immune tolerant phase
2. Immune clearance phase
3. Inactive carrier phase with or without reactivation

After acute infection of HBV, some patients may remain HBeAg positive with high levels of HBV DNA levels, little or no symptoms, normal ALT levels and minimal histological activity in the liver, this phenomenon is known as the immune tolerance phase. This phase is typical of infection in children and young adults. It usually lasts for 2-4 weeks, but can last for years in those who acquired the infection in the perinatal period (28). Individuals in this group are highly contagious and can transmit HBV easily. When the tolerogenic effect is lost during the immune tolerant phase, immune mediated lysis of infected hepatocytes become active and patients enter the second stage defined as immune clearance phase, the HBV DNA level decreases and ALT level increases. The duration of clearance lasts from months to years. This is followed by carrier stage, in which seroconversion of HBeAg to HBeAb occurs, HBV DNA becomes non-detectable or at low level and ALT is usually normal, reflecting very low or no replication of HBV and mild or no hepatic injury. The inactive carrier stage may last for even years or life time. Patients in this stage can have spontaneous resolution of hepatitis B and develops HBsAb, but a portion of them may undergo spontaneous or immunosuppression-induced reactivation of chronic hepatitis, features elevated ALT, high level of DNA, moderate to severe liver histological activity, and with or without HBeAg seroconversion.

CLINICAL SPECTRUM OF HBV INFECTION

ACUTE HEPATITIS B

Majority of HBV infection in children are asymptomatic versus those in adults, about 30 to 50% develop acute icteric hepatitis. Those who recover should acquire lifelong immunity. However, a subset of patients will be chronically infected and very few patients (0.1 – 0.5%) can develop fulminant hepatitis. In primary infection, HBsAg becomes detectable after 4 to 10 weeks of incubation period, followed by antibodies against the core antigen (HBcAb) in IgM form during the early period (7). Viremia is well established by the time HBsAg is detected (usually from 10^9 to 10^10 per milliliter) (29). Circulating HbeAg becomes detectable in most cases. When liver injury occurs in acute infection, ALT levels do not increase until after viral infection is well established, reflecting the time required to generate the T-cell-mediated immune response that triggers liver injury. Once this response has commenced, viral titres in blood and liver begins to drop. With clearance of the infection, HBsAg and HBeAg disappear, and free HBsAb becomes detectable. Presence of HBsAg for greater than 6 months implies progression to chronic infection. When persistent infection establishes, the serology markers like HBeAg, HBeAb and HBsAb can be positive or negative except HBsAg and HBcAb (IgM form) remain positive.

HBeAg positive chronic hepatitis B

Age at the time of infection is a strong determinant of chronicity, the earlier the acquisition of infection, the higher probability of developing chronic

infection. Levels of viremia in chronic infection are generally significantly lower than during acute infection. In adult acquired disease, the early phase of infection often is accompanied by significant disease activity with elevated ALT levels versus those who acquired the infection perinatally usually have normal ALT levels. Many patients with perinatal infection enter the immunoactive phase and develop HBeAg positive chronic hepatitis with elevated ALT levels only after 10-30 years of infection (30). A key event in natural history of progression is HBeAg seroconversion to HBeAb with marked reduction of HBV replication followed by gradual histological improvement (31). In studies, the observed clearance of HBeAg is about 50% and 70% within 5 and 10 years of diagnosis respectively (31). Most studies found the mean annual rate of spontaneous seroconversion is 8% to 15% in individuals with active liver disease, but those with normal ALT levels tend to have smaller annual conversion rate of 2% to 5%.

HBeAg negative chronic hepatitis B

These individuals have a naturally occurring mutant form of HBV that does not produce HBeAg, due to a mutation in the precore or core promoter region. Most frequent precore mutation is a G-A change at nucleotide 1896 (G1896A) which creates a stop codon and results in loss of HBeAg synthesis; the most common core promoter mutation involves a 2 nucleotide substitution at nucleotide 1762 and 1764 (32). HBeAg-negative carriers are a heterogeneous group and most of them have low viral HBV DNA levels, relatively normal levels of alanine aminotransferase, and a fair prognosis. However, in Asia, Middle East, Mediterranean basin and southern Europe,

about 15% to 20% of these carriers have elevated alanine aminotransferase and viral DNA (33). HBeAg-negative chronic hepatitis B (precore mutant) emerges as the predominant species during the course of typical HBV infection with wild-type virus and is selected during the immune clearance phase (HBeAg seroconversion) (34). There are 2 main patterns of disease activity in this subgroup of patients: 30%-40% of patients experience persistent elevated ALT levels (3-4 folds) and the remaining 60%-70% patients can have erratic ALT patterns with frequent flares. Sustained spontaneous remission is rare (6% to 15%) in these individuals, and spontaneous HBsAg clearance is only about 0.5% per year (35); hence, long-term prognosis is poorer among HBeAg-negative individuals than compare with their counterparts who are HBeAg-positive.

Inactive HBsAg carrier state:

Inactive HBsAg carrier state is diagnosed by HBeAg negativity with anti-HBe positivity, undetectable or low HBV DNA level, repeatedly normal ALT, and normal or minimal histological evidence of damage (36). The prognosis of the inactive carrier is generally good and well supported by long-term follow-up studies (37,38,39). An estimated 20% to 30% of HBsAg carriers may develop reactivation of hepatitis B with elevation of biochemical levels, high serum DNA level with or without sero-reversion to HBeAg. Recurrent episodes of reactivation or sustained reactivation can occur and contribute to progressive liver disease and decompensation. Frequently, HBV reactivation is usually asymptomatic, but it may mimic acute viral hepatitis. On the other hand, some carriers eventually become HBsAg negative and develop

HBsAb. It is reported that the incidence of delayed HBsAg clearance is close to 1% to 2% per year in Western countries, but only 0.05% to 0.8% per year in endemic areas where infection was often acquired during childhood. Reactivations of HBV replication in patients who receive immunosuppressive therapy or cytotoxic chemotherapy have been reported in the range of 20% to 50% in chronic carriers (40,41); from experience, the combined use of corticosteroid in chemotherapies significantly increases the risk of reactivation (40). However, these flares in the immunosuppressed individuals rarely result in significant hepatic decompensation.

Long-term Sequelae of Chronic Hepatitis B

Cirrhosis

Following the diagnosis of chronic hepatitis B, the survivals in these patients are estimated to be 100% at 5 years. However, cirrhosis and hepatoma are two major long-term complications of chronic HBV infection that significantly increases morbidity and mortality. In patients without cirrhosis, if untreated, the incidence of liver related death is low and ranges from 0 to 1.06 per 100 person years. The mortality rate at 5 years is 16% for those with compensated cirrhosis and is 65% to 86% for decompensated cirrhosis (42,43). In untreated individuals with predominantly HBeAg positive chronic hepatitis B, the incidence of cirrhosis ranges from 2 to 5.4 per 100 person years with a 5-year cumulative incidence of cirrhosis of 8% to 20% (45). A higher rate of cirrhosis has been reported in HBeAg-negative as compared to HBeAg-positive patients. Also, older age and persistent viral replication are predictors for

development of cirrhosis as well as mortality. Genotype C is associated with a higher risk of cirrhosis than genotype B based on studies in Asian patients(44). The presence of any other independent hepatotoxic factors such as alcohol ingestion, HCV co-infection can contribute to progression to cirrhosis. Once cirrhosis is established, individuals can decompensate over time.

Hepatocellular Carcinoma

The development of hepatocellular carcinoma (HCC) and liver failure are main cause of death from chronic hepatitis B. It is estimated that over 500,000 people die each year from the consequence of HBV infection (45). HCC incidence is three to six times higher in males than in females, suggesting a tumorigenic effect of androgens (47). Several studies have indicated that older age(>45 years) is an important determinant of HCC, this may either reflect a longer duration of viral infection and liver disease or agemay be an independent risk factor. Having a first degree relative with HCC, the presence of cirrhosis, and reversion activity are all thought to contribute to HCC development (47,48,49). Chronically infected subjects have a 100 times increased risk of hepatocellular carcinoma compare with non-carriers . A recent study suggested positive HBsAg increased one’s risk of developing HCC by 10 folds, and with positive HBeAg, HCC is significantly increased by 60 folds. Moreover, a detectable HBV DNA level yields a 4 fold increase risk of HCC (50). The additional use of alcohol, consumption of aflatoxin in diet and coinfection with HCV or HDV are independent factors for HCC in HBV infected patients. Unlike hepatitis C, development of HCC in hepatitis B patients does not require preceding cirrhosis. Hence, it is advocated that all

HBV infected patients, regardless of cirrhosis status, should get screening for HCC every 6 months with alpha-fetoprotein (AFP) and ultrasonogram abdomen.

VIRAL ANTIGENS AND HOST ANTIBODY RESPONSES:

Serological testing for the diagnosis of Hepatitis B virus infection involves measurement of a panel of distinct HBV-specific antigens and host antibodies that react to these antigens.(51,52,53). The interpretation of these tests can be complicated, and multiple possibilities exist based on the overall panel of responses. In general, the panel of responses can determine whether a patient is susceptible to infection, immune as a result of vaccination or resolved infection and acute or chronically infected.

Test Result	Interpretation
HBsAg (—) Total anti-HBc (—) anti-HBs (—)	Susceptible
HBsAg (—) Total anti-HBc (+) anti-HBs (+)	Immune due to natural infection
HBsAg (—) Total anti-HBc (—) anti-HBs (+)	Immune due to hepatitis B vaccination
HBsAg (+) Total anti-HBc (+) IgM anti-HBc (+) anti-HBs (—)	Acutely infected
HBsAg (+) Total anti-HBc (+) IgM anti-HBc (—) anti-HBs (—)	Chronically infected
HBsAg (—) Total anti-HBc (+) anti-HBs (—)	Four interpretations possible 1. Recovering from acute HBV infection 2. Distantly immune and test not sensitive enough to detect very low level of serum anti-HBs 3. Susceptible with a false positive anti-HBc 4. Chronic HBV infection with rare circumstance where HBV does not produce detectable HBsAg

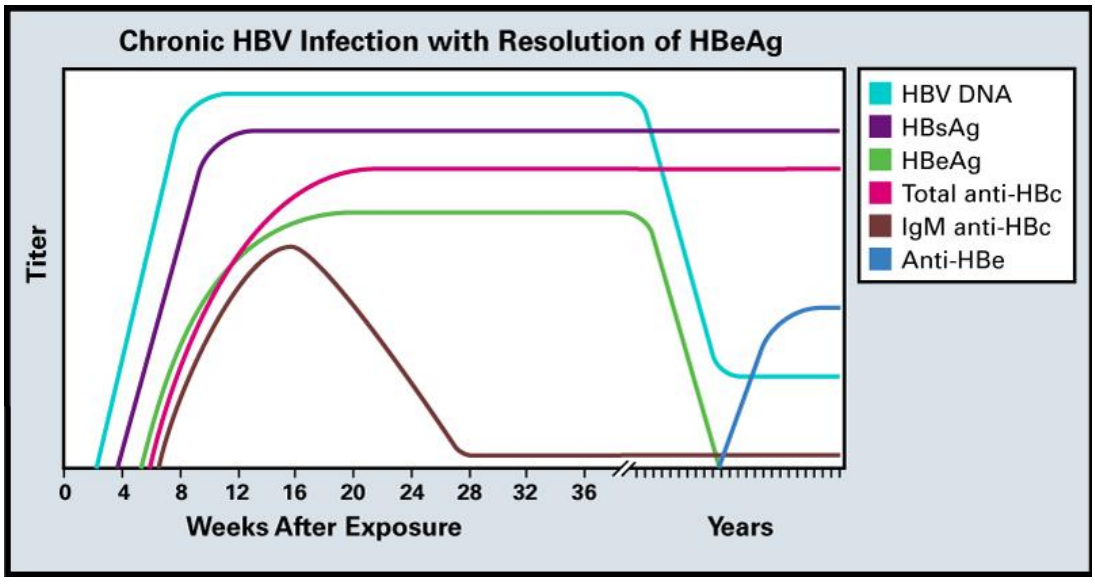
SEROLOGICAL RESPONSE TO ACUTE HBV INFECTION:

The incubation period typically consists of 8 to 12 weeks (51). During acute infection, the appearance of virological markers and host antibody response develop in a typical pattern. The first serological marker to appear is hepatitis B surface antigen (HBsAg), which can initially be detected in the serum from 1 to 12 weeks (30 to 60 days) after infection. Shortly thereafter, hepatitis B e antigen (HBeAg) generally becomes evident (54,55) . although serum assays will show presence of HBV DNA prior to the appearance of HBsAg or HBeAg, with HBV levels often exceeding 1000000000 virions/ml, this test is not generally performed for the diagnosis of acute HBv infection (56). About that time the clinical symptoms develop, antibody to hepatitis B core antigen appears (anti HBc), primarily detectable as IgM class (IgM anti HBc). In addition, with the onset of clinical symptoms, patients will have increases in serum hepatic aminotransferase levels that reflect hepatic injury. The degree of hepatic injury generally correlates directly with the vigor of the immune response (53). Although IgM anti HBc typically decline to undetectable levels within 6 months, IgG class persists indefinetly as a marker of past HBV infection.

SEROLOGICAL RESPONSE WITH RESOLVED HBV INFECTION

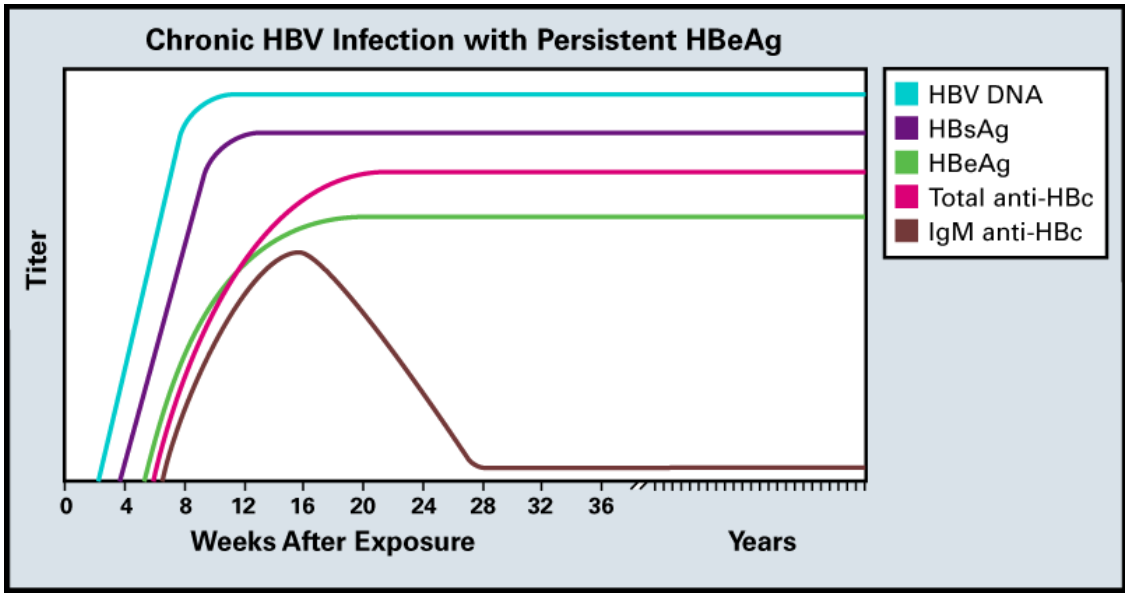
Following acute HBV infection, the evolution of the pattern of serological markers depends on the outcome of host immune response. The likelihood of resolving HBV infection correlates with their age and the strength of the initial immune response to HBV (52,53). Following an acute infection,

approximately 90% of adults will resolve the HBV infection whereas 30 to 40% of young children go in for chronicity. The weak immune response generated by young children acutely infected with HBV generally corresponds with minimal bleeding of the HBV infected hepatocytes; for this reason, clinical symptoms suggestive of acute HBV infection are frequently absent in this patient population (56). For those patients who resolve their infection, HBsAg disappears at about 3 to 6 months, often just prior to the detection of antibodies to hepatitis B surface antigen (anti HBs). The presence of anti-HBs following acute infection generally indicates recovery and protective immunity against re-infection. In addition, patients with resolution of infection have disappearance of HBeAg and development of antibodies to hepatitis B e antigen (anti HBe). Patients with resolved infection have persistence of anti HBs for life, but about 4 to 6 months after appearance of anti HBc predominantly consists of IgG. Some patients with self limited infection, however may still have HBV DNA in blood; whether the HBV DNA is part of intact virions is unknown (56,57).



SEROLOGICAL RESULT WITH CHRONIC HBV INFECTION:

Patients who develop persistant HBV infection have a serological response in the acute phase of HBV infection that is similar to patients who subsequently resolve the HBV infection. With persistent HBV infection, HBsAg and antiHBc (IgG antibodies) generally persist for life and HBV DNA can usually be detected by nucleic acid amplification methods. The presence of HBsAg for longer than 6 months after acute infection indicates chronic infection. The detection of HBsAg and the absence IgM anti HBc in a single serum specimen also generally indicates chronic HBV infection. Although most persons with chronic HBV infections are without symptoms, they are at risk for subsequently developing chronic hepatitis, cirrhosis and carcinoma (52). The continued presence of HBeAg generally reflects higher HBV DNA levels and greater infectiousness. Some patients with chronic HBV infection may have resolution of their HBeAg along with appearance of anti HBe and this usually correlates with low HBV levels and relatively normal levels of hepatic aminotransferase levels. Newer more sensitive PCR assays have shown that greater than 70% of persons who develop anti-HBe have persistent HBV DNA, typically in the range of 1000 to 100,000 mol/ml (56,59). In addition, some patients with chronic HBV infection have absent HBeAg, increased aminotransferase levels and relatively high HBV DNA levels; these findings generally occur in association with pre-core or core mutation. These mutations prevent or diminish HBeAg formation by an otherwise normally replicating HBV (56,60).



PREVENTION:

Three main strategies are available for the prevention of HBV infection:

(1) behavior modification to prevent disease transmission

(2) passive immunoprophylaxis

(3) active immunization.

Behavior Modification

Hepatitis B transmission can be reduced by avoiding unprotected penetrative anal and vaginal sex and oro-anal contact, or by using condoms if the partner is HBsAg positive or their status is unknown (61). [IIa, B].

Improved screening measures of blood products have reduced the risk of transfusion-associated hepatitis. Behavior modification is thought be more beneficial in developed countries than in developing countries, where neonates and children in early childhood are at the greatest risk of acquiring infection. In

these group, immunoprophylaxis, both passive and active, will be more effective.

Passive Immunoprophylaxis:

Hepatitis B Immune Globulin (HBIG) is a sterile solution of ready-made antibodies against hepatitis B. HBIG is prepared from human blood from selected donors who already have a high level of antibodies to hepatitis B and used in passive immunoprophylaxis.

Passive immunoprophylaxis is used in four situations

(1) newborns of mothers infected with hepatitis B

(2) after needlestick exposure

(3) after sexual exposure

(4) after liver transplantation.

Immunoprophylaxis is recommended for all infants born to HBsAg positive mothers. Current dosing recommendations are 0.13ml/kg HBIG immediately after delivery or within 12 hours after birth in combination with recombinant vaccine. The combination results in a higher-than-90% level of protection against perinatal acquisition of HBV (62). Between 3.7% to 9.9% of infants still acquire HBV infection perinatally from HBVinfection mothers, despite immunoprophylaxis (22-27). Failure of passive and active immunoprophyxis in this setting may be the result of in utero transmission of HBV infection, perinatal transmission related to a high inoculum, and/or the presence of surface gene escape mutants. However, the preventive effect of

HBIG administration before delivery needs to be confirmed by more study in the future.

Hepatitis B immune globulin remains a central component of prophylaxis in HBV-infected patients undergoing liver transplantation. HBIG monotherapy given at a high dosage can prevent recurrence in 65% to 80% of patients. Because the cost of long-term prophylaxis with high-dose HBIG is extremely high and combination therapy using HBIG with a nucleoside analog is more uniformly effective, the current protocol is combination HBIG with a nucleoside analog after liver transplantation. Thesecombination protocols have reduced the rate of virologic breakthrough to 10% or less (63).

Active Immunization

- The World Health Organisation recommends universal HBV vaccination.

- If universal vaccination is not pursued it should be offered to non-immune patients in most of the high risk groups (16,17,64,65).[Ia, A] The main exception is people born in countries of high endemicity but not at continuing risk who are being screened primarily to detect chronic HBV carriage (66,67). [IIa, B]

- HIV positive patients show a reduced response rate to the vaccine (approximately 40%) and initial responders can become anti-HBs-negative within a year (69,70). [IIa, B].

- There are three possible vaccination schedules for both the monovalent and the combined hepatitis A+B vaccines: 0 ,1, 6 months, 0, 1, 2 and 12 months (‘rapid course’) or 0, 1, 3 weeks, and 12 months (‘ultra-rapid course’) (61-65). [IIa, B] Non- or poor responders usually respond to further doses (up to three injections normal or double dose), ideally given as a repeat Course (63,64) [IIa, B]. Some newer vaccines are more immunogenic including Fendrix ™, which has a novel adjuvant and the pre-S-antigen-containing vaccines. Currently Fendrix is only licensed for use in patients with renal insufficiency and pre-S vaccines have not been launched commercially (58-62).

- If the primary course of vaccination is incomplete, the missing doses of vaccine needed to complete the course can be given up to four years later without the need to restart the full course [III, B]

- Some patients test anti-HBc positive but negative for anti-HBs and HBsAg. This could be due to either past infection or may be a false-positive test. A single hepatitis B vaccine dose will induce anti-HBs if there has been past natural HBV exposure (amnestic response, measured 4 weeks after single dose of HBV vaccine). If anti-HBs is still negative after a single booster, regard as non-infectious and give a full course of HBV vaccine [III.B]

- Recent evidence suggests that immuno-competent adults and children who have responded to a primary course of HBV vaccine (>10 IU/l) do not require booster doses for at least fifteen years [III, B].

However, immuno-compromised patients, such as those with HIV or renal failure, require booster doses of vaccine when the anti-HBs level falls below 10 IU/l [IIa, B].

Management of HBsAg-positive patients

General

- Patients should be advised to avoid unprotected sexual intercourse, including oro-anal contact until they have become non-infectious or their partners have been successfully vaccinated . [IIa,B]

- Patients should be given a detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partner(s), routes of transmission of infection and advised not to donate blood [III, B]

- Hepatitis B is a notifiable disease in many European countries (71).

- If not performed already, screen for other sexually transmitted diseases in cases thought to have been sexually acquired or if otherwise appropriate (29,33)[III,B]

- Other tests such as liver biopsy or assessment of liver fibrosis (for assessment of chronic disease) should be performed by specialists in this field (51)[IV, C]

Indications for therapy of Chronic Infection

- Treatment should normally be given in collaboration with a hepatologist or physician experienced in the management of chronic viral hepatitis [IV, C]. The decision to treat depends on pattern of disease, HBV-DNA level, and presence or absence of significant necro-inflammation and hepatic fibrosis. HBV-DNA thresholds of 2x10^4, 2x10^3 and 2x10^3 IU/ml, are often used for HBeAg+ve, chronic hepatitis, HBeAg –ve chronic hepatitis and cirrhosis respectively, for initiating therapy (72)

- Patients should be considered for therapy with lamivudine, adefovir, tenofovir, telbivudine, entecavir (or combinations of nucleos(t)ide analogues) or pegylated interferon [Ib, A]. Additional treatments that may soon be licensed in HBV monoinfection include emtricitabine (FTC) [Ib,A], clevudine [IIa,B] and valtorcitabine [III,C] (79-81). Treatment responders have long-termbenefits in terms of reduced liver damage and decreased risk of liver cancer (72-81)

- All patients should have an HIV test prior to starting HBV therapy because of the different treatment strategies required and the significant risk of antiretroviral- resistant HIV developing if lamivudine, tenofovir or entecavir are used as monotherapy [Ib,A] (72,73, 82-84).

- Lamivudine, emtricitabine and tenofovir will suppress hepatitis B viral replication during therapy of HIV and may delay liver damage if given as part of combination antiretroviral therapy. [Ib, A] (83-85).

- Lamivudine and emtricitabine should only be given to HIV+ patients in combination with tenofovir as part of HAART because of the high rate of resistance that occurs to these drugs if given as the only HBV-active agent [Ib,A] (83-85) .Entecavir should not be used in HIV+ patients without adequately suppressed HIV as it causes the M184V (lamivudine/emtricitabine) resistant mutation (82) and there is some evidence that telbivudine may also have HIV activity (86) [III,B]

- Adefovir can be used alone in HIV+ patients (87) [IIa,B]

- Specific therapy may not be indicated, based on the HBV-DNA viral load, unless de-compensated liver disease has ensued, but all HBsAg+ve patients should receive long-term follow-up due to the risk of liver cancer . Hepatitis A vaccination should be offered if non-immune, due to the worse prognosis of dual infection (88) [III,B]

Special situations

Pregnancy and Breastfeeding

- Vertical transmission (mother to infant) of infection occurs in 65-90% of pregnancies where the mother is HBeAg positive and in about ten percent of HBsAg positive, HBeAg negative mothers. Most (>90%) of infected infants become chronic carriers (89).

- Infants born to HBsAg positive mothers are vaccinated from birth, sometimes in combination with Hepatitis B specific Immunoglobulin (HBIG) 200 i.u. intramuscularly (89) [IIa,B]. This reduces vertical

transmission by approximately ninety percent. There is some evidence that lamivudine may further reduce vertical transmission if given to women with a high HBV-DNA viral load in the third trimester (90) [Ib, A]. However, if HBSIg is not available, vaccination alone prevents vertical transmission in 66-100% (89) [IIa, B]. Infants should be tested for hepatitis B (HBsAg and anti-HBs) 4-6 weeks after the final dose of vaccine [IV, C].

- Infected mothers should continue to breast feed as there is no additional risk of transmission.

Management of partners and other contacts

- Partner notification should be performed and documented and the outcome documented at subsequent follow-up. Contact tracing to include any sexual contact (penetrative vaginal or anal sex or oro/anal sex) or needle sharing partners during the period in which the index case is thought to have been infectious (91) [IIa, A]. The infectious period is from two weeks before the onset of jaundice until the patient becomes HBsAg negative. In cases of chronic infection trace contacts as far back as any episode of jaundice or to the time when the infection is thought to have been acquired although this may be impractical for periods of longer than two or three years [IV, C]. Arrange screening for hepatitis B of children who have been born to infectious women if the child was not vaccinated at birth [IV, C].

- If available, HBSIg 500 i.u. intramuscularly may be administered to a nonimmune contact after a single unprotected sexual exposure or parenteral exposure or needle-stick injury if the donor is known to be infectious. Passive immunization should be given as early as possible as it is of no use after more than seven days (92)[IIa,A]

- An accelerated course of recombinant vaccine should be offered to those given HBSIg plus all sexual and household contacts (at 0 ,1, 2,12 months or 0, 1, 3 weeks, 12 months) (83-87) [IIa,B]

- Avoid sexual contact, especially unprotected penetrative sex, until vaccination has been successful (anti-HBs titres >10i.u./l.) [IIa, B]. Condoms will reduce the rate of transmission of hepatitis B if the patient and partner continue to have sex [III, B].

Follow-up (81-92)

- Acute infection: regular Liver function tests (1-4 weekly) until normal. In view of the possibility of chronic infection, serum HBsAg should be repeated after six months even if the LFT is normal [III, B].

- Chronic infection: If untreated, patients should be regularly reviewed at intervals of one year or less, ideally by a physician with expertise in this disease [IV, C]

- Immunity after recovery from infection is lifelong in all but a very tiny minority [III, B].

MATERIALS & METHODS

STUDY POPULATION

Antenatal women attending out patient clinic at IOG

SAMPLE SIZE

All antenatal women attending out patient clinic within the study period.

INCLUSION CRITERIA

All antenatal women attending out patient clinic are included in the study

INVESTIGATIONS

Initial investigations: HbsAg and anti Hbc

Patients who are reactive to either of the above tests are subjected to the following tests

- Complete hemogram
- Liver function test
- Renal function test
- HBV DNA for viral load
- HBeAg

- Ultrasound Abdomen and pelvis
- Family screening

DATA COLLECTED

Socio demographic data, clinical data, laboratory data

DATA ANALYSIS

All the data collected were entered in MS EXCEL sheet and statistical analysis done by student t test (test of probability) and chi square test; p value below 0.01 taken as highly significant, < 0.05 as significant and >0.05 as non significant.

PRINCIPLE OF THE PROCEDURE

HBsAg:

Detected by using Hepanostika Test kit (ELISA) method. Hepanostika uniform II is a ELISA based on a one step ‘sandwich’ principle.

Anti HBc antibody

Wellcozyme anti HBc is an enzyme labeled immunoassay (EIA) kit for detection of antibody to hepatitis B core antigen.

HBeAg/Anti HBe

Wellcozyme HBeAg/Anti HBe is also an enzyme immunoassay to detect corresponding antigen and antibody

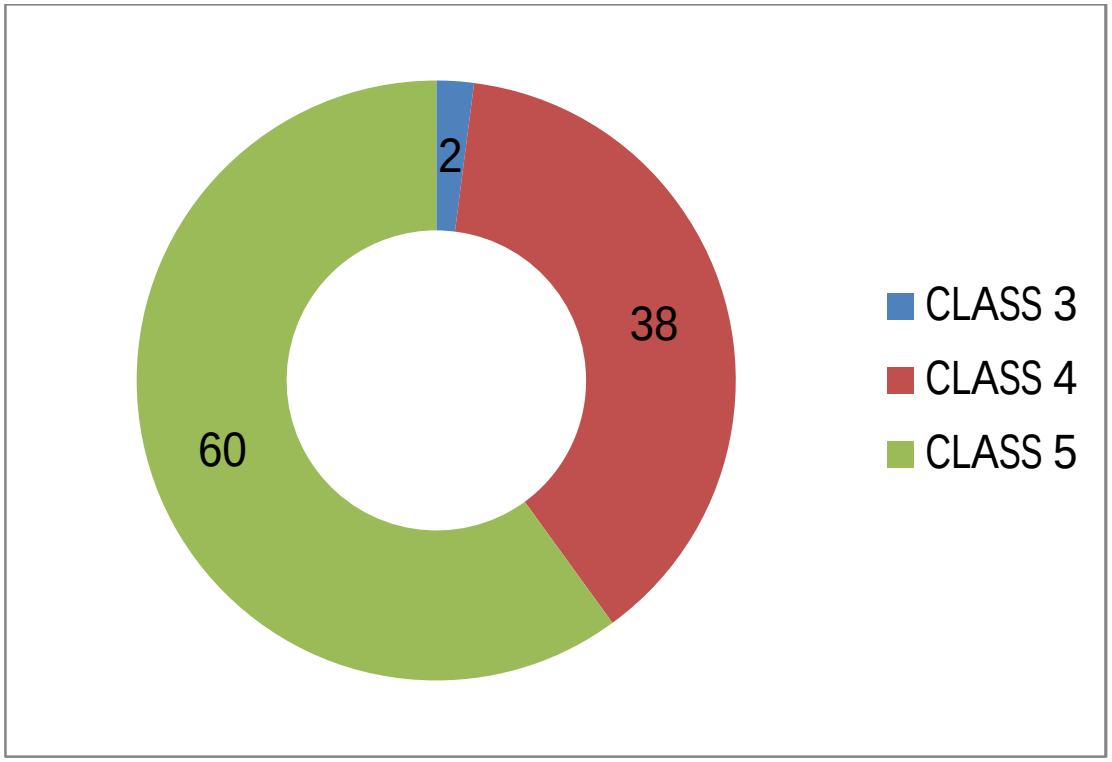
HBV DNA

Real time PCR technique. HBV DNA quantified using COBAS TAQ MAN kit.

OBSERVATION & RESULTS

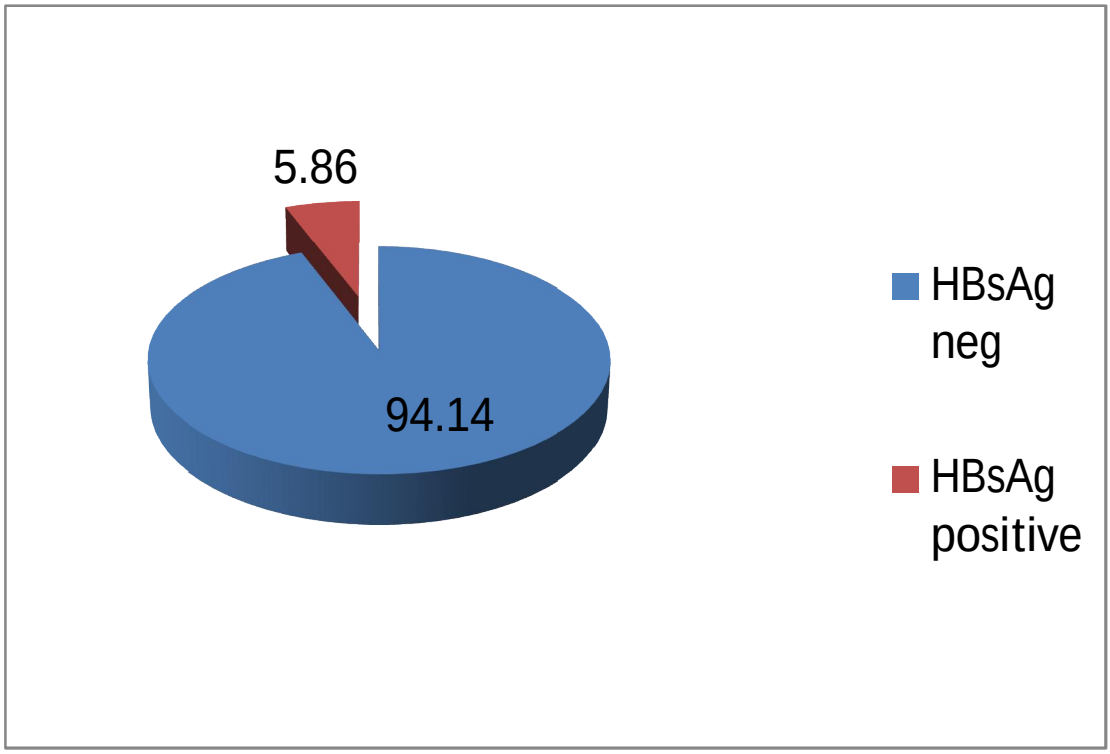
SOCIO-DEMOGRAPHIC DETAILS:

Of the 2730 women screened, 1228 (45%) were from urban sector and 1502 (55%) were from sub-urban and rural sectors. A majority of women belonged to low socio-economic class i.e. class 4 (1062; 38%) and class 5 (1583; 60%), only 3 women belonged to middle class according to revised Kuppuswamy's scale.



HBsAg PREVALENCE RATE:

Out of the 2730 women screened, 160 tested positive for hepatitis B surface antigen. Seroprevalence accounts to about 5.86%.



AGE WISE DISTRIBUTION:

The highest prevalence of HBsAg was observed in the age group 21-25 yrs (82/1082; 7.58%) followed by 26-30 yrs (45/864; 5.20%). The difference in HBsAg prevalence rate in different age groups was statistically significant with $p < 0.01$.

AGE GROUP	TOTAL	SEROPOSITIVES	SERO NEGATIVES
15 – 20 YRS	382	18 (4.7%)	364
21 – 25 YRS	1082	**82 (7.5%)**	1000
26 – 30 YRS	873	45 (5.1%)	828
31 – 35 YRS	302	11 (3.6%)	180
> 35 YRS	91	3 (3.2%0	88

PARITY DISTRIBUTION

The prevalence rate increased with increase in parity. It was highest among multigravida (98/1375; 7.12%), followed by second and primi gravid with a prevalence of 4.73% and 4.6% respectively. The prevalence rate in different group was statistically significant with $p < 0.05$.

GRAVIDITY	TOTAL	SERO POSITIVE	SERO NEGATIVE
PRIMIGRAVIDA	407	19 (4.6%)	388
SECONDGRAVIDA	948	43(4.7%)	905
MULTIGRAVIDA	1375	98(7.1%)	1277

TRIMESTER DISTRIBUTION

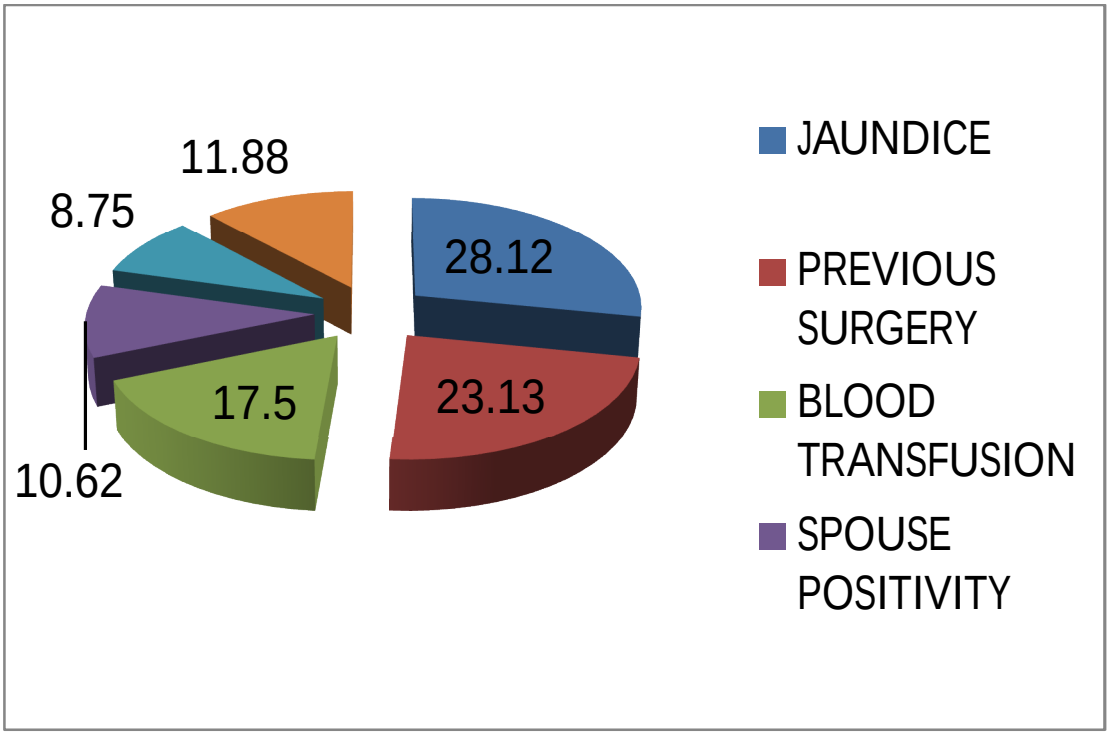
The seroprevalence in different trimesters were almost similar and statistically insignificant with p >0.05.

TRIMESTER	TOTAL	SERO POSITIVES	SERO NEGATIVES
FIRST	573	27 (4.7%)	546
SECOND	764	45 (5.8%)	719
THIRD	1665	88 (5.3%)	1577

RISK FACTORS FOR HBV INFECTION AMONG HBsAg POSITIVE WOMEN:

Previous history of jaundice was observed to be high i.e. 45/160(28.12%). 36 women had history of prior surgery, of which 27 of them had underwent obstetrical procedures including Dilatation & Curettage, Hysterotomy and Lower segment caesarean section. 9 patients underwent gastrointestinal, cardiothoracic and orthopaedic surgeries. 28 out of 160 gave history of blood transfusion within 5 yrs. History of tattooing observed in 14 HBsAg positive women.

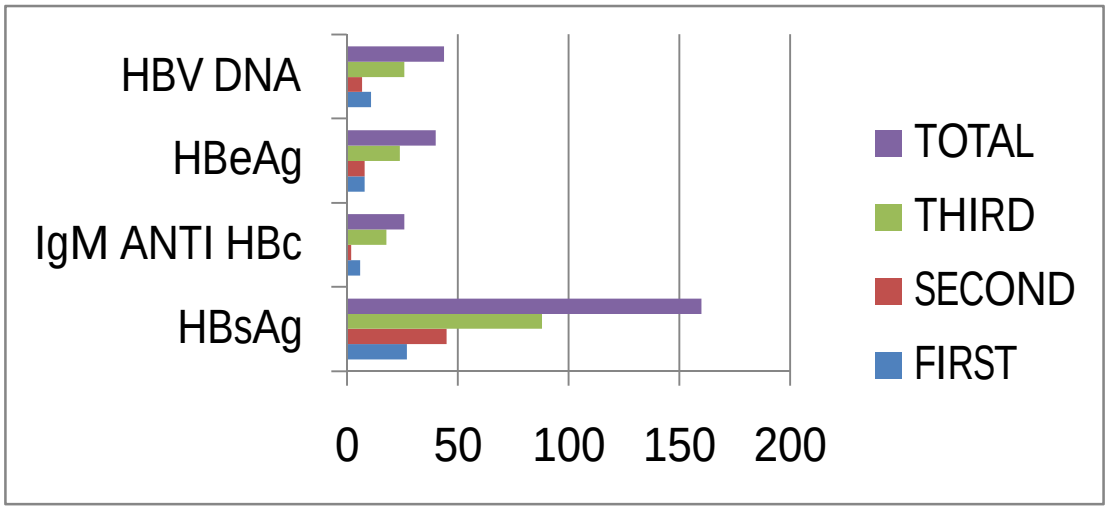
Regarding information on HBsAg positivity among husbands of seropositive women,17/160 were positive. Among them one was a health care worker. One women was a nurse in the seropositive group.



VIRAL MARKERS AND TRIMESTER DISTRIBUTION

40/160 HBsAg positive women tested positive for HBeAg antigen. Of these 18 had acute infection{IgM anti HBc positive} and 22 were chronic. 58 HBeAg negative patients were tested for HBV DNA and anti HBe antibody. 26 were positive for HBV DNA and anti HBe, 32 were positive for anti HBe alone. Only HBsAg positivity alone was observed in 62 women.

VIRAL MARKERS	I TRIMESTER	II TRIMESTER	III TRIMESTER
HBsAG	27 (16.8%)	45 (28.1%)	88 (55%)
IgM ANTI-HBc	6 (23.6%)	2 (7.6%)	18 (69.2%)
HBeAg	8 (20%)	8 (20%)	24 (60%)
HBV DNA	11 (25%)	7 (15.9%)	26 (59%)



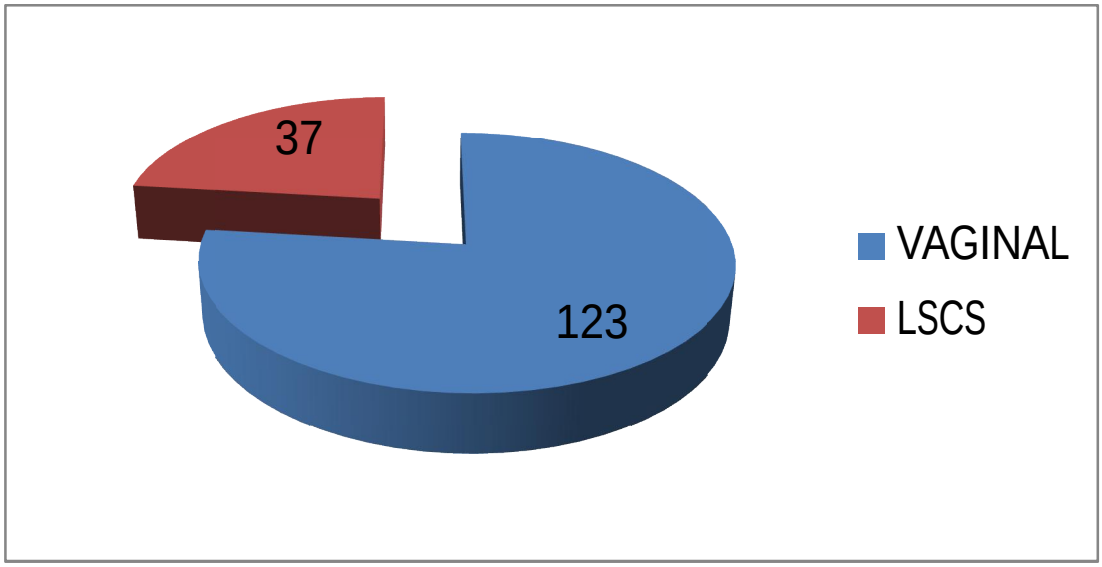
VERTICAL TRANSMISSION

Transmission among babies was tested by cord blood HBsAg positivity at birth. Of the 18 acutely infected patients , 10 babies were affected.14 babies were affected among the chronic infection group. Mothers who were positive for HBV DNA and anti HBe antibody transmitted their infection to 16 babies. Only 1 baby was affected in the only anti HBe positive group. 3 babies were affected in isolated HBsAg positivity. The difference in transmission among babies in the various serological groups was statistically significant with a p value < 0.01.

SEROLOGY	PATIENTS	SERO POSITIVE BABIES	SERO NEGATIVE BABIES
ACUTE HEPATITIS (HBsAg, ANTI HBc IgM,HBeAG, HBV DNA POSITIVE)	18	10(53%)	8
CHRONIC HEPATITIS (HBsAg, HBeAg POSITIVE)	22	14(63.6%)	8
HBsAg, HBV DNA, ANTI HBe POSITIVE HBeAg NEGATIVE	26	16(61.4%)	10
HBsAg, ANTI HBe POSITIVE HBeAg, HBV DNA NEGATIVE	32	1(3.12%)	31
HBsAg POSITIVE	62	3(4.8%)	59

MODE OF DELIVERY

123 out of the 160 positive women delivered normally. 37 underwent lower segment cesarian section all for obstetrical indications.



PERINATAL OUTCOME

BABY WEIGHT	TOTAL NUMBER	PRETERM	TERM
< 2 KGS	18	11	7
2 TO 3 KGS	128	22	106
>3 KGS	14	-	14

1 among the term babies whose mother was HBeAg and HBV DNA positive in the third trimester was an IUD. Other causes for intrauterine term IUD like gestational diabetes, pre eclampsia, ante partum hemorrhage[abrutio placenta], nuchal cord and congenital anomalies were ruled out .

There were 56 neonatal admissions . Of them 29 were pre term , 11 were low birth weight term babies, 16 were birth aspyxiants.

Comparative of Seroprevalence rates of HBs Ag and HBeAg Among pregnant women in different populations.

Author, Year and reference	Population studied	Number of persons screened	HBsAg +ve (%)	HBeAg +Ve (% of HBsAg positive)
Mohammed et.al. 2008	Saudi Arabia		1.60	
Bertolini et.al. 2006	Brazil	3,188	1.50	
Khalil et.al. 2005	Saudi Arabia		2.44	0.15
Panda et.al.1991	India	8,431	2.6	12.5
Gill et.al. 1995	India	2,000	5.0	12.0
Biswas et.al.1989	India	1,000	2.3	48
Mittal et.al.	India	850	6.3	18
Manisha et.al. 2008	Allahabad, India	4,000	0.9	57
Present Study, 2010	Chennai, Tamilnadu, India	2,730	5.86	25

DISCUSSION

In this study the sero prevalence of HBsAg among pregnant women was found to be 5.86%. sero epidemiological studies of different populations show variations and differences. These differences can be attributed to various factors like type of population studied, geographical region, genetic factors and socio economic conditions. The HBsAg positivity in antenatal pregnant women in India ranges from 1 to 12.3% with a mean of 4.22%. Similar study conducted by manisha et al in 2008 at Allahabad reported 0.9 % prevalence. Other studies conducted in india between 1987 – 2000. Nayak et al (3.7%), panda et al (2.6%), gill et al (5.0%) , biswas et al (2.3%) and mittal et al observed 6.3% prevalence rates.

A significant difference and increase in prevalence rate was observed with increasing age among the seropositive group as reported in many other Indian and foreign studies, except for the Allahabad study (manisha et al in 2008) where a slight non significant decline was observed with increasing age group. Also a higher and statistically significant frequency of HBsAg positivity was observed in multigravida.

According to Centres for Disease Control guidelines, every pregnant women should be tested for HBsAg during each pregnancy. Our results show that the HBsAg tests have been done more in the third trimester. This is due to lack of awareness among pregnant women.

In our study, even though history of jaundice was observed in high percentage among the seropositive women, such icteric episodes could not be

taken as a significant risk factor as the cause of the icteric episode cannot be ascertained. However there were a small percentage of seropositive patients without any identifiable risk factors. Also a significant percentage among the seronegative group had one or two risk factors.

HBeAg positivity rate among HBsAg positive antenatal women have shown geographical variations in different parts of india as reported by Shenoy et al. HBeAg positivity in our study {25%} was 50 % less study conducted by Manisha et al at Allahabad.

Mothers who were affected in the 3rd trimester transmitted infection to the babies moré than the mothers infected in 1st and 2nd trimester. Similar results were found in other studies. A significant association between e antigen positivity and HBV DNA and transmission of infection to babies was observed in our study . This once again proves that the combination of e antigen and HBV DNA is a more sensitive indicator of vertical transmission.

Two women had high titres of HBV DNA (> 100000) and presence of HBeAg, detected in the third trimester, both of them were started on LAMIVUDINE 100 mg twice daily and advised to continue 6 weeks postpartum.

Transmission rates and significance depending on the mode of delivery could not be ascertained because all patients who were screened did not deliver in our institution, hence baby follow up was practically difficult for all patients.

CONCLUSION

- The seroprevalence rate for Hepatitis B in antenatal women was found to be 5.86% in our study. This places our part of the country in the intermediate endemicity zone.

- Statistically significant difference was observed in age and parity distribution, whereas no such difference was observed in trimester distribution due to lack of awareness about Hepatitis B among pregnant women.

- HBeAg and HBV DNA positivity in antenatal mothers increases the risk of vertical transmission. This has been proved in our study which showed significantly higher rates of transmission and adverse perinatal outcome in third trimester infections.

- As evident from our study vertical transmission and health care providers are at risk of contracting Hepatitis B infection, hence routine screening for all antenatal women and routine immunization for all health care workers is recommended

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No: 04425305301
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CERTIFICATE OF APPROVAL

To
Dr. A. Anusha Raaj
PG in MD OG
Institute of Obstetrics & Gynaecology,
Egmore, Chennai-8

Dear Dr. A. Anusha Raaj

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled " Prevalence and clinical study of hepatitis B in antenatal women attending outpatient clinic at Institute of Obstetrics and Gynaecology / Madras Medical College, Chennai " No. 08102011.

The following members of Ethics Committee were present in the meeting held on 20.10.2011 conducted at Madras Medical College, Chennai -3

1.	Prof. S.K. Rajan. MD	-- Chairperson
2.	Prof. A. Sundaram, MD Vice Principal , Madras Medical College, Chennai -3	-- Member Secretary
3.	Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	-- Member
4.	Prof. C. Rajendiran, MD Director , Institute of Internal Medicine, MMC, Ch-3	-- Member
5.	Thiru. A. Ulaganathan Administrative Officer, MMC, Chennai -3	-- Layperson
6.	Thiru. S. Govindasamy . BA.BL	-- Lawyer
7.	Tmt. Arnold Soulina MA	-- Social Scientist
8.	Prof. Shanta Ravishankar Prof of Neuropathology, M M C, Chennai -3	-- Member

We approve the proposal to be conducted in its presented form

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee

PATIENT CONSENT FORM

STUDY TITLE :

"PREVALENCE AND CLINICAL STUDY OF HEPATITIS B IN ANTENATAL WOMEN ATTENDING OUT PATIENT CLINIC AT I.O.G."

STUDY CENTRE : Department of obstetrics and gynecology,
Institute of Obstetrics and Gynecology, Egmore, Chennai- 8

Patient may check (✓) these boxes.

PARTICIPANT NAME : **AGE:** **I.D.NO. :**

I confirm that I have understood the purpose of the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason, without my legal rights being affected. ☐

I understand that investigator, the institution, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I hereby consent to, undergo complete physical examination, and diagnostic tests including hematological, biochemical, radiological and urine examinations ☐

I hereby consent to participate in this study of **PREVALENCE AND CLINICAL STUDY OF HEPATITIS B IN ANTENATAL WOMEN ATTENDING OUT PATIENT CLINIC AT I.O.G."** ☐

Signature of the Patient : ..... Place ..... Date .....

Address .....

Signature of the Witness : ..... Place ..... Date .....

Signature of the Investigator : ..... Place ..... Date .....

மகளிர் மகப்பேறு மருத்துவமனைக்கு வரும் கர்ப்பிணி பெண்களுக்கு மஞ்சள் காமாலை தொற்று உள்ளதா என்பது பற்றி ஆய்வு செய்தல்.

ஆய்வு செய்யும் இடம் : மகப்பேறு அரசு மருத்துவமனை
எழும்பூர், சென்னை - 08.

பங்கு பெறுபவரின் பெயர் :

பங்கு பெறுபவரின் எண் :

பங்கு பெறுபவரின் வயது :

பங்கு பெறுபவர் இதனை ( ) குறிக்கவும்.

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விபரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்று அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் ஆய்வு மேற்கொள்ளும் நிறுவனம், நன்நடத்தை நெறிமுறைகள் குழு, ஒழுங்குமுறை ஆணையங்கள் என அறிந்து கொள்கிறேன். நான் ஆய்விலிருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையோ, முடிவுகளையோ அறிவியல் சார்ந்த தேவைகளுக்காக பயன்படத்திக் கொள்ள மறுக்கமாட்டேன். மூணாம் நபர்களுக்கு தரப்படும் அல்லது பிரசுரிக்கப்படுத்த ஏதேனும் தகவல்களில் என் தனிப்பட்ட அடையாளம் வெளிப்படுத்தபடமாட்டாது எனவும் நான் புரிந்து கொண்டேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம் ..... இடம் ..... தேதி

கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம் ..... தேதி

ஆய்வாளரின் பெயர் .....

INFORMATION SHEET

Principal Investigator : Dr.A.Anusha Raaj

Contact Number : 9884601229

Institution : Institute of Obstetrics and Gynaecology, Egmore, Chennai-600 008.

Prevalence and Clinical Study of Hepatitis B in Antenatal Women attending out patient clinic at I.O.G.

Hepatitis B infection in pregnancy gains importance because of its increased rate of perinatal transmission and maternal morbidity. In pregnancy it may lead to liver cell failure, chronic liver disease, severe IUGR, Preterm labour, sudden IUD and still birth. Hence it is essential to screen all antenatal women to identify hepatitis B infected individuals and provide effective immunization to the neonates of infected individuals.

The study is done to know the prevalence, cause, treatment and outcome of Hepatitis B infection in pregnancy. Appropriate blood investigations and ultrasound examination will be done.

There is no known risk to the patient. The benefit arising from the study will be useful in early diagnosis of this condition and prevention of its consequences by appropriate management. The identity of the individual will be kept confidential.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator **Signature of participant**

Date:

S.NO: **DATE:**

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

NAME: AGE/SEX: OP NO:

OCCUPATION: LITERACY STATE:

W/O: HUSBAND'S OCC:

ADDRESS & MOBILE NO:

S.E STATUS: CLASS I/CLASS II/CLASS III/CLASS IV

MENSTRUAL HISTORY:

OBSTETRIC CODE & HISTORY:

H/O SHT/T2DM/PT/BA/EPILEPSY: YES/NO

H/O MEDICAL ILLNESS IN FAMILY: YES/NO {IF YES ELABORATE}

H/O JAUNDICE/LIV DS/PIH: YES/NO {IF YES ELABORATE}

DURATION: MONTHS/YEARS

TREATMENT: NATIVE/ALLOPATHY

ABDOMEN DISTENSION: YES/NO

ABDOMEN PAIN: YES/NO

PEDAL EDEMA: YES/NO

OLIGURIA: YES/NO

GI BLEED: YES/NO

H/O JAUNDICE IN FAMILY: YES/NO

H/O VACCINATION FOR HEPATITIS B: YES/NO

H/O VACCINATION FOR HEP B BY SPOUSE/FAMILY: YES/NO

H/O BLOOD TRANSFUSION: YES/NO

H/O TATOOING: YES/NO

H/O TRANSPLANTATION: YES/NO

H/O CHRONIC DRUG INTAKE: YES/NO

H/O SURGICAL ILLNESS: YES/NO

EXAMINATON:

PALLOR: YES/NO
JAUNDICE: YES/NO
PEDAL EDEMA: YES/NO
SIGNS OF LIVER CELL FAILURE: YES/NO

CVS:

RS:

P/A:

CNS:

MASTER CHART – 1

SOCIO DEMOGRAPHIC DETAILS

H. NO	NAME	AGE	OCC	S.OCC	SE CLASS	GRAVIDITY	TRIME-STER
254	SUMATHY	3	1	2	5	2	2
261	THYBUNISHA	2	1	2	5	1	1
219	KALAIRANI	2	1	2	5	2	1
385	LAKSHMI	4	1	2	5	3	1
396	YAMINI	2	1	3	4	2	2
487	SHARMILA	2	1	2	5	1	3
512	KANNIAMMAL	3	1	2	5	3	3
528	INDUMALAR	2	1	3	4	1	2
580	RADHA	1	1	3	4	1	2
603	PREMA	3	1	2	5	4	3
634	SUMATHY	2	1	2	5	2	1
637	GRACY	5	1	3	4	1	2
646	JAYANTHI	2	1	3	5	2	2
656	MARIAMMAL	2	1	2	5	1	2
670	BANUPRIYA	2	1	3	5	1	3
677	HEMAVATHY	2	1	3	5	1	2
695	VEERALAKSHMI	3	1	2	5	2	3
721	KAVITHA	2	1	3	5	2	3
736	REKHA	2	1	2	5	2	2
771	SUMATHY	4	4	3	4	2	2
836	BHARANI DEVI	2	1	3	4	1	3
860	JENNIFER	3	1	2	5	2	1
816	JAYANTHI	2	1	2	5	3	2
937	GEETHA	4	1	2	5	2	1
954	PADMAVATHY	3	1	2	5	2	2
981	RAJESHWARI	2	1	2	5	2	3
1000	BAGYALAKSHMI	2	3	3	4	1	2

H. NO	NAME	AGE	OCC	S.OCC	SE CLASS	GRAVIDITY	TRIME-STER
1006	SHANTHY	3	1	3	4	1	2
1008	KALAIYARASI	1	1	3	4	1	1
1110	THILAGAVATHY	3	1	2	5	3	2
1182	SHANTHY	2	1	3	4	1	3
1185	MEENATCHI	1	1	3	4	1	1
1194	PRIYA	2	1	2	5	2	2
1208	VASANTHI	5	1	2	5	3	3
1215	CHITRA	2	1	2	5	1	3
1255	GEETHA	2	1	3	4	1	3
1265	JEGADEESWARI	2	1	3	4	2	3
1282	SHAJITHA	1	1	2	5	1	2
1289	MAHESWARI	2	1	3	4	2	3
1306	MENAKA	2	1	2	5	1	1
1319	TAMILSELVI	2	1	2	5	2	3
1322	ASIA BEGUM	2	1	2	5	1	3
1341	GEETHA	2	1	2	5	1	3
1343	LATHA	2	1	3	4	2	2
1388	SARANYA	3	1	3	4	2	1
1429	SUGANYA	4	1	3	4	2	3
1430	RAJALAKSHMI	2	1	3	4	2	3
1431	SUDHA	1	1	2	5	1	2
1437	BHOOPATHY	2	1	2	5	2	3
1450	SANGEETHA	1	1	4	4	3	3
1453	AMUDHA	2	1	3	4	1	3
1457	KALAIVANI	3	1	3	4	1	3
1465	FATHIMA	2	1	3	4	1	1
1473	RANGAMMAL	2	1	2	5	3	3
1482	SANDIYA	2	1	2	5	3	3
1497	SARASWATHI	1	1	2	5	2	3
1520	NATHIYA	1	1	3	4	1	3
1526	REVATHI	2	1	3	5	1	3

H. NO	NAME	AGE	OCC	S.OCC	SE CLASS	GRAVIDITY	TRIME-STER
1538	MEENATCHI	2	1	2	5	1	1
1540	CHITRA	1	1	3	5	1	2
1542	MAHALAKSHMI	2	1	2	5	1	1
1543	DHANALAKSHMI	4	1	3	5	2	3
1544	GOVINDAMMAL	2	1	2	5	2	3
1558	FATHIMA	2	1	2	5	3	3
1568	PADMAVATHY	2	1	3	4	1	3
1581	SHOBANA	3	1	2	5	1	2
1592	ILAKIYA	2	1	2	5	1	3
1600	SUDHA	3	1	2	5	4	3
1612	RUTH BABY	3	1	2	5	1	3
1613	SASIKALA	2	1	2	5	1	2
1627	ASSERIEN	1	1	2	5	1	3
1651	SANDRA	1	1	2	5	3	2
1713	NIRMALA	2	1	3	4	2	3
1757	SARASWATHI	3	1	3	4	2	2
1768	RESHMA	2	1	3	4	4	3
1777	DHANALAKSHMI	2	1	3	4	2	3
1790	SHAKILA	3	1	3	4	5	2
1886	PUSHPALATHA	3	1	2	5	2	1
1949	LAKSHMI	2	1	3	4	2	3
2032	MEGALA	3	1	2	5	2	3
2037	SANGEETHA	2	1	3	4	2	3
2039	AMLORPAVAMARY	4	1	3	4	1	2
2071	BANUMATHY	3	1	3	4	5	2
2075	FATHIMA	3	1	3	4	3	1
2085	VIJAYALAKSHMI	3	1	3	4	1	2
2109	JAYANTHI	3	1	2	5	2	3
2115	GOMATHI	2	1	2	5	3	3
2139	KAVITHA	3	1	3	4	3	2
2152	NARMADHA	2	1	3	4	3	2

H. NO	NAME	AGE	OCC	S.OCC	SE CLASS	GRAVIDITY	TRIME-STER
2191	NAGAMMAL	1	1	2	5	1	2
2210	MANJULA	3	1	2	5	2	2
2264	SUNDARI	2	1	3	4	1	2
2290	RENUKA	4	3	3	3	2	2
2331	SASIKALA	2	1	2	5	1	3
2334	BALAKAVITHA	3	1	3	4	2	1
2398	DEEPALAKSHMI	2	1	3	4	2	1
2401	AMULMANI	5	3	2	4	2	3
2405	JAYA	3	1	3	4	2	3
2414	SUGUNA	3	1	3	4	2	1
2436	RANI	3	1	2	5	3	3
2439	SANGEETHA	2	1	3	4	2	1
2479	SARANYA	2	1	2	5	3	1
2483	SUJATHA	2	1	3	4	1	3
2489	RAMEEZABAI	2	1	2	5	2	1
2490	UMAPRIYA	4	1	3	4	1	3
2510	KUMARI	1	1	2	5	2	3
2514	SUBEDHA	3	1	3	4	2	3
2519	JAYANTHI	3	1	3	4	3	3
2536	KAVITHA	2	1	3	4	2	3
2546	SATHIYA	2	1	3	5	2	3
2564	KODEESWARI	3	1	3	4	1	2
2603	MARAGATHAM	3	1	3	4	2	3
114	LAKSHMI	1	1	3	4	1	1
115	PUSHPALATHA	2	1	3	5	1	1
116	NAZIRA BANU	2	1	2	5	2	2
117	SARITHA	2	1	3	4	3	1
118	RADHIKA	3	1	2	5	1	2
119	VIJAYALAKSHMI	4	1	3	4	4	1
120	JAMUNA	1	1	3	4	1	2
122	KALAVATHI	2	1	2	5	3	3

H. NO	NAME	AGE	OCC	S.OCC	SE CLASS	GRAVIDITY	TRIME-STER
123	SUBHA	2	1	2	5	1	1
124	SHABHANA	3	1	3	4	2	1
125	KODEESWARI	2	1	2	5	2	1
130	MARAGATHAM	3	1	3	4	2	3
137	DEVIKA	1	1	2	5	1	3
139	MANJULA	2	1	2	5	1	3
4	VIJAYALAKSHMI	4	1	2	5	2	2
9	USHA	2	1	2	5	1	1
11	MALLIGA	2	1	3	4	2	3
25	MALATHY	3	1	2	5	2	2
34	SHEELA	2	1	2	5	1	3
35	NAVANEETHAM	2	1	2	5	4	2
47	MALINI	2	1	2	5	1	2
54	JOTHI	3	1	2	5	2	3
63	KRISHNAVENI	2	1	2	5	1	3
70	EZHILARASI	2	1	3	4	1	3
82	SENTHAMARAI	3	1	3	4	2	3
98	REENA	3	1	2	5	1	3
103	SUGUNA	2	1	2	5	1	3
104	SUMATHY	1	1	2	5	1	2
106	SUMATHY	3	1	3	4	2	3
110	SHYLAJA	2	1	2	5	1	3
2607	CHITRA	2	1	2	5	1	2
2615	KANCHANA	2	1	2	5	1	3
2616	PANDISELVI	1	1	2	5	1	3
2618	BACKIALAKSHMI	2	1	2	5	1	3
2620	JAYANTHI	2	1	2	5	1	3
2622	VIMALA	2	1	3	4	1	3
2628	ASHIYA BEGUM	3	1	2	5	1	3
2632	DHANALAKSHMI	3	1	2	5	1	3
2633	MUTHULAKSHMI	3	1	3	4	2	3

H. NO	NAME	AGE	OCC	S.OCC	SE CLASS	GRAVIDITY	TRIME-STER
2636	RAJESHWARI	2	1	2	5	1	3
2641	KALAIARASI	1	1	2	5	1	3
2643	SANDYA	3	1	2	5	1	3
2650	KAVITHA	4	1	2	5	1	3
2652	SHANTHI	2	1	2	5	2	3
2674	SIVAGAMI	3	1	2	5	2	3
2680	VIMALA	3	1	2	5	4	3
2684	SANGEETHA	2	1	2	5	1	3
2691	SUNDARI	2	1	2	5	1	3

MASTER CHART – 2

PAST HISTORY

NAME	SPOUSE	TATOOING	JAUNDICE	SURGERY	TRANSFUSION	HBsAG	ANTI HBC	IgM HBc
SUMATHY	2	2	1	0	2	1	2	2
THYBUNISHA	2	2	2	0	2	1	1	1
KALAIRANI	2	2	2	0	2	1	2	2
LAKSHMI	2	2	2	0	2	1	2	2
YAMINI	2	2	2	0	2	1	2	2
SHARMILA	2	2	2	0	2	1	2	2
KANNIAMMAL	2	1	2	0	1	1	2	2
INDUMALAR	2	2	2	0	2	1	2	2
RADHA	2	2	2	0	2	1	2	2
PREMA	1	2	2	0	2	1	1	1
SUMATHY	2	2	1	0	2	1	2	2
GRACY	2	2	1	0	2	1	2	2
JAYANTHI	2	2	1	0	2	1	2	2
MARIAMMAL	2	2	1	0	2	1	2	2
BANUPRIYA	2	2	2	0	2	1	2	2
HEMAVATHY	2	2	1	0	2	1	2	2
VEERALAKSHMI	2	2	2	0	2	1	1	1
KAVITHA	1	2	1	0	2	1	2	2
REKHA	2	2	2	1	2	1	2	2

NAME	SPOUSE	TATOOING	JAUNDICE	SURGERY	TRANSFUSION	HBsAG	ANTI HBC	IgM HBc
SUMATHY	2	2	2	0	2	1	2	2
BHARANI DEVI	1	2	1	0	2	1	1	1
JENNIFER	2	2	2	0	1	1	2	2
JAYANTHI	2	2	2	0	2	1	2	2
GEETHA	2	2	2	1	2	1	2	2
PADMAVATHY	2	2	2	0	2	1	2	2
RAJESHWARI	2	2	1	0	2	1	2	2
BAGYALAKSHMI	2	2	1	2	2	1	1	2
SHANTHY	2	2	2	0	2	1	2	2
KALAIYARASI	2	2	2	0	2	1	2	2
THILAGAVATHY	2	2	2	0	2	1	2	2
SHANTHY	2	2	1	0	2	1	1	1
MEENATCHI	2	2	2	0	2	1	1	1
PRIYA	2	2	1	0	2	1	2	2
VASANTHI	2	2	2	0	2	1	2	2
CHITRA	2	1	2	0	2	1	2	2
GEETHA	1	2	2	0	2	1	2	2
JEGADEESWARI	2	2	2	1	2	1	2	2
SHAJITHA	2	1	2	0	2	1	2	2
MAHESWARI	1	2	2	0	1	1	2	2
MENAKA	2	2	2	0	2	1	2	2

NAME	SPOUSE	TATOOING	JAUNDICE	SURGERY	TRANSFUSION	HBsAG	ANTI HBC	IgM HBc
TAMILSELVI	2	2	2	0	2	1	2	2
ASIA BEGUM	2	1	2	0	2	1	2	2
GEETHA	1	2	2	0	2	1	2	2
LATHA	2	2	2	1	2	1	2	2
SARANYA	1	2	2	0	2	1	2	2
SUGANYA	2	2	2	1	2	1	2	2
RAJALAKSHMI	2	2	1	1	2	1	2	2
SUDHA	2	2	2	0	2	1	2	2
BHOOPATHY	2	2	1	0	2	1	1	2
SANGEETHA	2	2	2	0	2	1	2	2
AMUDHA	2	2	2	0	2	1	2	2
KALAIVANI	2	2	2	2	1	1	2	2
FATHIMA	2	2	2	0	2	1	2	2
RANGAMMAL	2	2	2	1	1	1	1	2
SANDIYA	2	2	1	0	2	1	1	2
SARASWATHI	2	1	2	0	2	1	2	2
NATHIYA	2	2	1	0	2	1	2	2
REVATHI	2	2	2	0	2	1	2	2
MEENATCHI	2	1	2	0	2	1	2	2
CHITRA	1	2	2	0	2	1	1	1
MAHALAKSHMI	2	2	2	2	1	1	2	2

NAME	SPOUSE	TATOOING	JAUNDICE	SURGERY	TRANSFUSION	HBsAG	ANTI HBC	IgM HBc
DHANALAKSHMI	2	1	2	1	1	1	2	2
GOVINDAMMAL	2	2	2	0	2	1	2	2
FATHIMA	2	2	2	0	2	1	2	2
PADMAVATHY	2	2	2	0	2	1	2	2
SHOBANA	2	2	2	1	1	1	2	2
ILAKIYA	2	2	1	0	2	1	1	2
SUDHA	2	2	2	0	1	1	2	2
RUTH BABY	1	2	1	0	2	1	2	2
SASIKALA	2	2	2	0	2	1	2	2
ASSERIEN	2	2	2	0	2	1	1	1
SANDRA	2	2	1	2	1	1	2	2
NIRMALA	2	2	2	0	1	1	2	2
SARASWATHI	2	2	2	0	2	1	2	2
RESHMA	2	2	2	1	2	1	2	2
DHANALAKSHMI	2	2	2	0	2	1	2	2
SHAKILA	2	2	2	0	2	1	2	2
PUSHPALATHA	2	2	2	1	1	1	2	2
LAKSHMI	2	2	1	1	2	1	1	1
MEGALA	2	2	2	1	2	1	2	2
SANGEETHA	2	2	2	0	2	1	2	2
AMLORPAVAMARY	1	2	2	0	2	1	2	2

NAME	SPOUSE	TATOOING	JAUNDICE	SURGERY	TRANSFUSION	HBsAG	ANTI HBC	IgM HBc
BANUMATHY	2	2	1	1	1	1	2	2
FATHIMA	2	2	2	2	1	1	2	2
VIJAYALAKSHMI	2	2	1	0	2	1	2	2
JAYANTHI	2	2	1	1	2	1	1	2
GOMATHI	2	1	1	0	2	1	2	2
KAVITHA	2	2	1	1	2	1	1	2
NARMADHA	2	2	2	1	1	1	2	2
NAGAMMAL	2	2	2	0	2	1	2	2
MANJULA	2	2	2	1	2	1	2	2
SUNDARI	2	2	2	0	2	1	2	2
RENUKA	1	2	2	1	2	1	2	2
SASIKALA	2	2	1	0	2	1	1	2
BALAKAVITHA	2	1	1	0	2	1	1	1
DEEPALAKSHMI	1	2	2	0	2	1	2	2
AMULMANI	2	2	1	0	2	1	2	2
JAYA	1	2	1	0	2	1	2	2
SUGUNA	2	1	1	0	2	1	2	2
RANI	2	2	2	0	2	1	2	2
SANGEETHA	2	2	1	0	2	1	1	1
SARANYA	2	2	2	1	1	1	2	2
SUJATHA	2	2	1	0	2	1	2	2

NAME	SPOUSE	TATOOING	JAUNDICE	SURGERY	TRANSFUSION	HBsAG	ANTI HBC	IgM HBc
RAMEEZABAI	2	2	1	1	2	1	2	2
UMAPRIYA	2	2	1	0	1	1	2	2
KUMARI	2	2	2	0	2	1	2	2
SUBEDHA	2	2	2	1	2	1	2	2
JAYANTHI	2	2	2	0	2	1	2	2
KAVITHA	2	2	1	0	2	1	2	2
SATHIYA	1	2	1	0	2	1	2	2
KODEESWARI	2	2	1	0	2	1	1	1
MARAGATHAM	2	2	1	1	1	1	2	2
LAKSHMI	2	2	2	2	1	1	2	2
PUSHPALATHA	2	2	2	0	1	1	2	2
NAZIRA BANU	2	1	2	0	2	1	1	2
SARITHA	2	2	2	1	1	1	2	2
RADHIKA	2	2	2	2	1	1	2	2
VIJAYALAKSHMI	2	2	2	1	1	1	2	2
JAMUNA	2	2	2	0	2	1	2	2
KALAVATHI	2	1	2	0	2	1	2	2
SUBHA	2	2	2	2	1	1	2	2
SHABHANA	2	2	2	0	2	1	2	2
KODEESWARI	2	1	2	1	2	1	2	2
MARAGATHAM	2	2	2	0	2	1	1	1

NAME	SPOUSE	TATOOING	JAUNDICE	SURGERY	TRANSFUSION	HBsAG	ANTI HBC	IgM HBc
DEVIKA	2	2	2	0	2	1	2	2
MANJULA	2	2	1	0	1	1	2	2
VIJAYALAKSHMI	2	2	1	0	1	1	1	2
USHA	2	2	2	0	2	1	2	2
MALLIGA	2	2	2	0	2	1	2	1
MALATHY	2	2	2	0	2	1	2	1
SHEELA	2	2	1	0	2	1	2	1
NAVANEETHAM	2	2	2	0	2	1	1	2
MALINI	2	2	1	0	1	1	2	1
JOTHI	2	2	2	0	2	1	2	1
KRISHNAVENI	1	2	1	1	2	1	1	1
EZHILARASI	2	2	2	0	2	1	1	1
SENTHAMARAI	2	2	2	0	2	1	2	1
REENA	2	2	2	0	2	1	2	1
SUGUNA	2	2	1	0	2	1	2	1
SUMATHY	2	2	2	0	2	1	1	1
SUMATHY	2	2	2	0	2	1	1	2
SHYLAJA	2	1	2	0	2	1	2	2
CHITRA	2	2	1	0	2	1	2	2
KANCHANA	1	2	2	0	2	1	2	2
PANDISELVI	1	1	2	0	2	1	2	2

NAME	SPOUSE	TATOOING	JAUNDICE	SURGERY	TRANSFUSION	HBsAG	ANTI HBC	IgM HBc
BACKIALAKSHMI	1	2	2	0	2	1	2	2
JAYANTHI	2	2	2	0	2	1	2	2
VIMALA	2	2	2	0	2	1	2	2
ASHIYA BEGUM	2	2	2	0	2	1	2	2
DHANALAKSHMI	2	2	2	0	2	1	2	2
MUTHULAKSHMI	2	2	2	0	2	1	1	1
RAJESHWARI	2	2	2	0	2	1	2	2
KALAIARASI	2	2	2	0	2	1	2	2
SANDYA	2	2	2	0	2	1	1	2
KAVITHA	2	2	2	2	1	1	2	2
SHANTHI	2	2	2	0	2	1	1	1
SIVAGAMI	2	2	2	0	2	1	2	2
VIMALA	2	2	2	0	2	1	2	2
SANGEETHA	2	2	2	0	2	1	2	2
SUNDARI	2	2	1	0	2	1	2	2

MASTER CHART -3

VIRAL MARKERS & BABY DETAILS

NAME	HBeAg	ANTI Hbe	HBV DNA	DELI-VERY	BABY	BABY WEIGHT
SUMATHY	2	2	N	1	2	2
THYBUNISHA	1	2	2341	2	2	2
KALAIRANI	2	2	N	1	2	2
LAKSHMI	2	1	11236	1	1	2
YAMINI	2	1	N	1	2	2
SHARMILA	1	2	N	1	1	2
KANNIAMMAL	2	2	N	1	2	2
INDUMALAR	2	1	N	1	2	2
RADHA	2	2	N	1	1	2
PREMA	1	2	112362	1	2	2
SUMATHY	2	2	N	1	2	2
GRACY	2	1	N	1	2	2
JAYANTHI	2	2	N	1	2	2
MARIAMMAL	2	1	N	1	2	2
BANUPRIYA	2	2	N	1	2	2
HEMAVATHY	2	2	N	1	2	1
VEERALAKSHMI	1	2	111123	1	1	2
KAVITHA	1	2	5625	1	2	2
REKHA	2	1	N	2	2	2
SUMATHY	2	1	13872	1	1	3
BHARANI DEVI	1	2	11657	1	1	2
JENNIFER	2	2	N	1	2	2
JAYANTHI	2	2	N	1	2	2
GEETHA	1	2	N	2	1	2
PADMAVATHY	2	2	N	1	2	1

NAME	HBeAg	ANTI Hbe	HBV DNA	DELI-VERY	BABY	BABY WEIGHT
RAJESHWARI	2	1	N	1	2	2
BAGYALAKSHMI	2	2	N	1	2	1
SHANTHY	2	1	5712	2	1	1
KALAIYARASI	2	2	N	1	2	2
THILAGAVATHY	2	2	N	1	2	2
SHANTHY	1	2	5437	2	1	2
MEENATCHI	1	2	N	2	2	2
PRIYA	2	1	N	1	2	3
VASANTHI	1	1	N	2	2	2
CHITRA	2	1	3249	1	1	2
GEETHA	1	2	N	1	2	1
JEGADEESWARI	2	2	N	2	2	2
SHAJITHA	2	2	N	2	2	2
MAHESWARI	2	1	N	2	2	2
MENAKA	2	2	N	1	2	2
TAMILSELVI	2	1	N	1	2	2
ASIA BEGUM	1	2	N	1	1	2
GEETHA	1	2	N	1	2	2
LATHA	2	2	N	1	2	2
SARANYA	2	2	N	1	2	2
SUGANYA	2	1	6243	1	1	3
RAJALAKSHMI	2	1	N	1	2	1
SUDHA	2	2	N	2	2	1
BHOOPATHY	2	2	N	1	2	2
SANGEETHA	2	2	N	1	2	2
AMUDHA	2	1	761	1	2	2
KALAIVANI	2	1	N	1	2	2
FATHIMA	2	2	N	1	1	2

NAME	HBeAg	ANTI Hbe	HBV DNA	DELI-VERY	BABY	BABY WEIGHT
RANGAMMAL	1	2	N	1	1	2
SANDIYA	2	1	N	1	2	2
SARASWATHI	2	2	N	1	2	2
NATHIYA	2	1	2130	1	2	2
REVATHI	2	2	N	2	2	2
MEENATCHI	2	2	N	1	2	2
CHITRA	1	2	N	1	2	2
MAHALAKSHMI	2	1	N	1	2	2
DHANALAKSHMI	2	2	N	2	2	1
GOVINDAMMAL	1	2	N	1	2	2
FATHIMA	1	2	N	1	2	2
PADMAVATHY	2	2	N	1	2	2
SHOBANA	2	1	7914	1	1	2
ILAKIYA	2	1	N	1	2	3
SUDHA	2	2	N	1	2	2
RUTH BABY	1	2	N	1	2	2
SASIKALA	2	1	N	1	2	2
ASSERIEN	1	2	11352	1	1	2
SANDRA	2	1	1472	1	2	2
NIRMALA	2	2	N	1	2	3
SARASWATHI	1	2	N	1	1	2
RESHMA	2	1	N	2	2	2
DHANALAKSHMI	2	1	N	1	2	2
SHAKILA	2	1	7635	1	1	1
PUSHPALATHA	1	2	N	2	2	2
LAKSHMI	1	2	N	2	1	1
MEGALA	2	2	N	2	2	2
SANGEETHA	2	1	N	2	2	2

NAME	HBeAg	ANTI Hbe	HBV DNA	DELI-VERY	BABY	BABY WEIGHT
AMLORPAVAMARY	2	2	N	1	2	1
BANUMATHY	2	1	2081	2	1	2
FATHIMA	2	2	N	1	2	2
VIJAYALAKSHMI	1	2	N	2	2	2
JAYANTHI	2	2	N	2	2	2
GOMATHI	2	2	N	1	2	2
KAVITHA	2	1	N	2	2	3
NARMADHA	1	2	N	2	1	2
NAGAMMAL	2	2	N	1	2	2
MANJULA	2	1	21721	2	1	2
SUNDARI	2	1	N	1	2	2
RENUKA	2	1	N	2	2	2
SASIKALA	2	2	N	1	2	2
BALAKAVITHA	1	2	1165	1	2	3
DEEPALAKSHMI	2	2	N	1	2	2
AMULMANI	2	1	11231	1	1	2
JAYA	1	2	N	1	2	2
SUGUNA	2	1	N	1	2	2
RANI	2	2	N	1	2	2
SANGEETHA	1	2	N	1	2	2
SARANYA	2	1	N	2	2	1
SUJATHA	2	2	N	1	2	2
RAMEEZABAI	2	1	11162	2	1	2
UMAPRIYA	2	2	N	1	2	2
KUMARI	2	1	N	1	2	3
SUBEDHA	1	2	N	2	1	2
JAYANTHI	2	2	N	2	2	2
KAVITHA	2	2	N	1	2	2

NAME	HBeAg	ANTI Hbe	HBV DNA	DELI-VERY	BABY	BABY WEIGHT
SATHIYA	2	1	N	1	2	2
KODEESWARI	1	2	N	1	1	2
MARAGATHAM	2	2	N	2	2	2
LAKSHMI	2	2	N	1	2	1
PUSHPALATHA	1	2	N	1	2	2
NAZIRA BANU	2	2	N	1	2	2
SARITHA	2	2	N	1	2	2
RADHIKA	2	1	2628	1	1	2
VIJAYALAKSHMI	2	1	N	1	2	3
JAMUNA	2	2	N	1	2	3
KALAVATHI	1	2	N	1	2	1
SUBHA	2	2	N	1	2	3
SHABHANA	2	1	1921	1	2	2
KODEESWARI	2	1	N	1	2	2
MARAGATHAM	1	2	N	2	IUD	1
DEVIKA	2	2	N	1	2	2
MANJULA	2	1	1378	1	2	2
VIJAYALAKSHMI	2	2	3.18	1	2	2
USHA	1	2	N	1	1	2
MALLIGA	2	1	N	1	2	2
MALATHY	2	2	N	2	2	2
SHEELA	2	1	31821	1	1	2
NAVANEETHAM	2	2	N	2	2	2
MALINI	1	2	N	1	2	2
JOTHI	2	2	N	1	2	1
KRISHNAVENI	1	2	1000	1	1	2
EZHILARASI	1	2	1123	1	2	2
SENTHAMARAI	2	2	N	2	2	2

NAME	HBeAg	ANTI Hbe	HBV DNA	DELI-VERY	BABY	BABY WEIGHT
REENA	2	1	1323	1	2	3
SUGUNA	2	1	N	1	2	1
SUMATHY	1	2	1032	1	1	2
SUMATHY	2	2	N	1	2	2
SHYLAJA	2	1	N	1	2	2
CHITRA	2	2	N	1	2	2
KANCHANA	1	2	N	1	1	2
PANDISELVI	2	2	N	2	2	2
BACKIALAKSHMI	2	1	812	1	2	2
JAYANTHI	2	2	N	1	2	2
VIMALA	2	1	1192	1	2	2
ASHIYA BEGUM	2	1	N	1	2	2
DHANALAKSHMI	2	1	N	1	2	3
MUTHULAKSHMI	1	2	N	1	2	2
RAJESHWARI	2	1	4694	1	1	2
KALAIARASI	2	1	5328	2	1	2
SANDYA	2	1	N	1	2	2
KAVITHA	2	1	122	1	2	2
SHANTHI	1	2	N	1	1	2
SIVAGAMI	2	1	N	2	1	2
VIMALA	2	1	122	1	2	3
SANGEETHA	2	1	1421	1	1	2
SUNDARI	2	2	N	1	2	1

KEY TO MASTER CHART

AGE:
15-20 YRS : 1
21-25 YRS : 2
26-30 YRS : 3
31-35 YRS : 4
>35 YRS : 5

OCCUPATION:
Unemployed : 1
Labourer : 2
Self-employed : 3
Health care worker : 4

SOCIO-ECONOMIC CLASS : REVISED KUPPUSWAMY SCALE

GRAVIDITY:
Primigravida : 1
II gravida : 2
Multigravida : 3, 4 and 5

TRIMESTER:
First : 1
Second : 2
Third : 3

RISK FACTORS:
Presence of risk factor : 1
Absence : 2

SURGERY:
No surgery : 0
Obstetric procedure : 1
Other surgery : 2

SEROLOGY;
Positive :1
Negative : 2

DELIVERY:
Vaginal delivery : 1
LSCS : 2

BABY WEIGHT:
< 2 kgs : 1
2-3 kgs : 2
>3 kgs : 3

ABBREVIATIONS

HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HDV	Hepatitis D virus
HEV	Hepatitis E virus
HIV	Human Immunodeficiency Virus
HCC	Hepato Cellular Carcinoma
DNA	Deoxyribonucleic acid
RNA	Ribonucleic acid
HBsAg	Hepatitis b surface antigen
ANTI HBc	Antibody against core antigen (total & IgM)
HBeAg	Hepatitis B e antigen
ANTI HBe	Antibody against e antigen
HBV DNA	Hepatitis B Deoxyribonucleic acid
SGOT	Alanine aminotransferase
SGPT	Aspartate aminotransferase
SAP	Serum Alkaline phosphatase
LFT	Liver function tests
ELISA	Enzyme Linked Immunosorbent Assay
RFT	Renal function tests
PCR	Polymerase Chain Reaction